

```

(FILE 'HOME' ENTERED AT 12:41:27 ON 13 SEP 2000)

FILE 'REGISTRY' ENTERED AT 12:42:20 ON 13 SEP 2000
L1      STRUCTURE UPLOADED
L2      4 S L1 SSS SAM
L3      100 S L1 SSS FULL

FILE 'STNGUIDE' ENTERED AT 12:50:55 ON 13 SEP 2000

FILE 'REGISTRY' ENTERED AT 12:55:16 ON 13 SEP 2000

FILE 'MARPAT' ENTERED AT 12:56:56 ON 13 SEP 2000

FILE 'REGISTRY' ENTERED AT 12:57:39 ON 13 SEP 2000

FILE 'MARPAT' ENTERED AT 12:58:20 ON 13 SEP 2000

FILE 'CAPLUS' ENTERED AT 13:00:06 ON 13 SEP 2000
L4      186 S L3
L5      0 S 2' DEOXY 2' FLUORO RIBONUCLEOSIDE AND L4
L6      0 S 2' (W)DEOXY (W)2' (W) FLUORO (2W)NUCLEOSIDE

FILE 'REGISTRY' ENTERED AT 13:06:52 ON 13 SEP 2000

FILE 'HCAPLUS' ENTERED AT 13:08:09 ON 13 SEP 2000

FILE 'REGISTRY' ENTERED AT 13:08:44 ON 13 SEP 2000

FILE 'HCAPLUS' ENTERED AT 13:08:55 ON 13 SEP 2000

FILE 'REGISTRY' ENTERED AT 13:10:53 ON 13 SEP 2000

FILE 'HCAPLUS' ENTERED AT 13:11:13 ON 13 SEP 2000

FILE 'CAPLUS' ENTERED AT 13:11:58 ON 13 SEP 2000

FILE 'HCAPLUS' ENTERED AT 13:12:10 ON 13 SEP 2000

FILE 'MARPAT' ENTERED AT 13:13:57 ON 13 SEP 2000

FILE 'CAPLUS' ENTERED AT 13:14:19 ON 13 SEP 2000

FILE 'MARPAT' ENTERED AT 13:14:20 ON 13 SEP 2000

FILE 'CAPLUS' ENTERED AT 13:14:54 ON 13 SEP 2000

FILE 'MARPAT' ENTERED AT 13:15:06 ON 13 SEP 2000
L7      0 S 2 (2W)DEOXY 2 (2W) FLUORO (2W) RIBONUCLEOSIDE
L8      0 S NUCLEOSIED
L9      1 S NUCLEOSIDE
L10     0 S L9 AND L4

=> s nucleoside

NUCLEOSIDE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.80	275.71
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-12.78

FILE 'HCAPLUS' ENTERED AT 13:20:49 ON 13 SEP 2000  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1967 - 13 Sep 2000 VOL 133 ISS 12  
FILE LAST UPDATED: 12 Sep 2000 (20000912/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in HCAPLUS on STN.

=> s nucleoside

NUCLEOSIDE IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> e nucleoside

E1	1	NUCLEOSIDATIONS/BI
E2	2	NUCLEOSIDATO/BI
E3	32473	--> NUCLEOSIDE/BI
E4	1	NUCLEOSIDEA/BI
E5	1	NUCLEOSIDEACETIC/BI
E6	1	NUCLEOSIDEAMIDOPHOSPHITES/BI
E7	1	NUCLEOSIDEASE/BI
E8	2	NUCLEOSIDECARBOXYLATE/BI
E9	1	NUCLEOSIDECOMPONENT/BI
E10	1	NUCLEOSIDECYCLOPHOSPHATES/BI
E11	3	NUCLEOSIDEDI/BI
E12	7	NUCLEOSIDEDIPHOSPHATASE/BI

=> s e3 and 14

32473 NUCLEOSIDE/BI  
186 L3  
L11 115 NUCLEOSIDE/BI AND L4

=> s 2'-deoxy-2'-fluoro ribonucleoside

5613964 2  
31827 'DEOXY'  
5613964 '2'  
55706 FLUORO  
2861 RIBONUCLEOSIDE  
L12 0 2'-DEOXY-2'-FLUORO RIBONUCLEOSIDE  
(2(W)'DEOXY'(W)'2'(W)FLUORO(W)RIBONUCLEOSIDE)

=> d l11 71-80 ibib abs hitstr

L11 ANSWER 71 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1987:168640 HCAPLUS

DOCUMENT NUMBER: 106:168640

TITLE: Inhibition of DNA primase by **nucleoside**  
triphosphates and their arabinofuranosyl analogs

AUTHOR(S): Parker, William B.; Cheng, Yung Chi

CORPORATE SOURCE: Dep. Pharmacol., Univ. North Carolina, Chapel Hill,  
NC, 27514, USA

SOURCE: Mol. Pharmacol. (1987), 31(2), 146-51

CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB DNA primase [64885-96-7] produces an RNA oligomer of approx. 10 bases,  
which is required by DNA polymerase .alpha. (EC 2.7.7.7) for the  
initiation of DNA synthesis. DNA primase was partially purified from  
acute lymphocytic leukemia cells from patients by using several  
chromatog.

columns. Poly(dT) and poly(dC), but not poly(dA) or poly(dG), were good  
templates for ribonucleoside triphosphate (rNTP)-dependent DNA synthesis  
(i.e., DNA primase activity), and they were used in the study of the  
effect of natural and arabinofuranosyl **nucleoside** triphosphates  
on DNA primase activity. The Km for GTP [86-01-1] in the poly(dC)  
primase assay was .apprx.175 .mu.M. All noncomplementary natural rNTPs  
and deoxyribonucleoside triphosphates (dNTPs) inhibited poly(dC) primase  
activity to a similar extent (Ki values of ATP [56-65-5] and CTP  
[65-47-4] were 610 and 517 .mu.M, resp.). 1-.beta.-D-  
Arabinofuranosylcytosine 5'-triphosphate (araCTP) [13191-15-6] and  
9-.beta.-D-arabinofuranosyladenine 5'-triphosphate (araATP) [3714-60-1]  
were more potent inhibitors of poly(dC) primase activity than were CTP

and

ATP (Ki values were .apprx.125 .mu.M). AraCTP, araATP, CTP, and ATP  
inhibited DNA primase activity in a manner competitive with GTP. The  
concn. required to inhibit poly(dC) DNA primase activity by 50% was detd.  
for a no. of arabinofuranosyl **nucleoside** triphosphate analogs,  
and the relative potency of inhibition of DNA primase activity was as  
follows: rNTP = dNTP = 5-aza-dCTP [72052-96-1] < ara-5-azaCTP  
[98204-39-8] = araTTP [66097-68-5] = araATP = araCTP < 2-fluoro-araATP  
[74832-57-8] = 2'-azido-2'-deoxy-araCTP [59652-91-4] < 2'-fluoro-araTTP  
[79551-89-6] = 2'-fluoro-5-iodo-araCTP [79570-63-1] =  
2'-fluoro-5-methyl-araCTP [79570-62-0]. In the poly(dT) primase assay  
ATP did not follow classic Michaelis-Menten kinetics (ATP exhibited pos.  
cooperativity with a Hill coeff. of 2.0). However, this assay was very  
sensitive to araCTP (apparent Ki of 25 .mu.M). In summary, these expts.  
suggested that DNA primase is controlled by the levels of ribonucleoside  
triphosphates, and that the perturbation of these pools by any agent

could

lead to the inhibition of DNA primase and thereby inhibit DNA synthesis.  
Furthermore, aranucleoside triphosphate analogs directly inhibited DNA  
primase, and it is possible that this effect may contribute to the  
cytotoxicity of these compds.

IT 79551-89-6

RL: BIOL (Biological study)

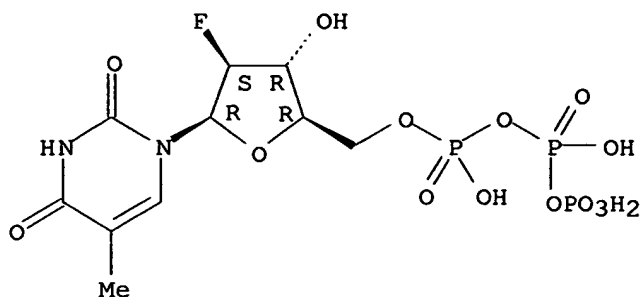
(DNA primase inhibition by, cytotoxic mechanism in relation to)

RN 79551-89-6 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-

[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 72 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1987:152055 HCAPLUS  
DOCUMENT NUMBER: 106:152055  
TITLE: Human immunodeficiency virus reverse transcriptase.  
General properties and its interactions with

**nucleoside** triphosphate analogs  
AUTHOR(S): Cheng, Yung Chi; Dutschman, Ginger E.; Bastow,  
Kenneth

F.; Sarngadharan, M. G.; Ting, Robert Y. C.  
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC,  
27514, USA

SOURCE: J. Biol. Chem. (1987), 262(5), 2187-9  
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Using affinity purified human immunodeficiency virus (HIV) reverse transcriptase, the reaction assay conditions were detd. The optimum incorporation of dTMP into the (rA)n(dT)10 template with HIV reverse transcriptase required 6 mM MgCl2 with 80 mM KCl. The template specificity of HIV reverse transcriptase was quite different from those of the human DNA polymerase-.gamma.-assocd. reverse transcriptase or avian virus reverse transcriptase. The preferential inhibition of HIV reverse transcriptase as compared to human DNA polymerase-.gamma.-assocd. reverse transcriptase was obsd. with several **nucleoside** analog triphosphates. The Ki values for thymidine triphosphate analogs with HIV reverse transcriptase were in the range 5-13 nM with decreasing effectiveness for 3'-fluoro > 3'-amino > 2',3'-dideoxy > 3'-azido groups. This study provided information on the structure-activity relations of the triphosphate analogs inhibitory effects on HIV reverse transcriptase vs. human DNA polymerase-.gamma.-assocd. reverse transcriptase, and the possible mechanisms of action of 3'-azidothymidine and the 2',3'-dideoxynucleosides, and also identified other **nucleoside** analogs for possible development as inhibitors of HIV.

IT 79551-89-6

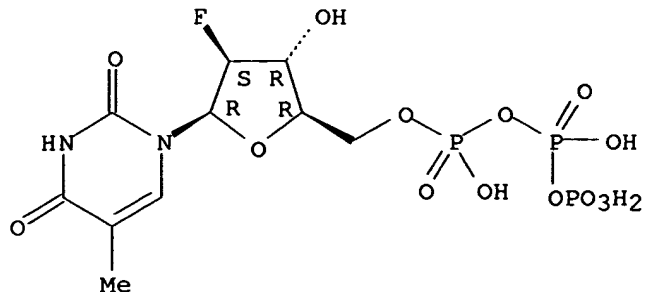
RL: BIOL (Biological study)

(reverse transcriptase of human immunodeficiency virus inhibition by)

RN 79551-89-6 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 73 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1987:113538 HCAPLUS

DOCUMENT NUMBER: 106:113538

TITLE: Anti-herpes virus compositions containing  
5-substituted (1,2'-deoxy-2'-substituted  
.beta.-D-arabinofuranosyl)pyrimidine nucleosides

INVENTOR(S): Lopez, Carlos; Watanabe, Kyoichi A.; Reichman, Uri;  
Fox, Jack J.

PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA

SOURCE: U.S., 11 p. Cont. of U.S. Ser. No. 366,104,  
abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

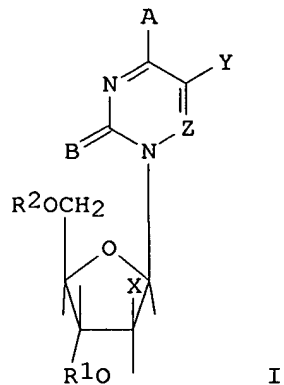
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4594339	A	19860610	US 1984-621875	19840618
PRIORITY APPLN. INFO.:			US 1982-366104	19820406

GI



I

AB The title compds. (I; A = OR<sub>3</sub>, SR<sub>3</sub>, NR<sub>3</sub>R<sub>4</sub>, or NH-acyl; R<sub>3</sub>, R<sub>4</sub> = H, C<sub>1</sub>-7 alkyl, aralkyl, aryl; B = O, S; X = H, alkylsulfonyl, arylsulfonyl; Y = halo, NH<sub>2</sub>, monoalkyl, etc.; Z = methyne, N; R<sub>1</sub>, R<sub>2</sub> = H, acyl, aroyl) are effective in controlling herpes virus. Thus, 88 I compds. are claimed, and the preps. of some of them are described. The inhibitory activities of some I compds. such as

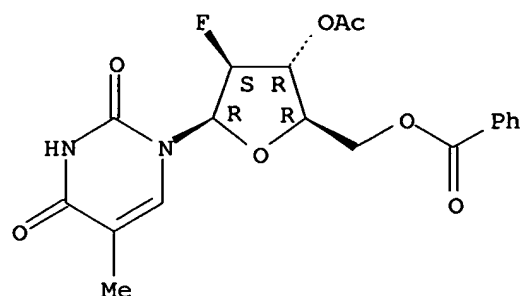
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine against herpes simplex virus type 1 and 2 were demonstrated in vitro.

IT 69124-04-5

RL: RCT (Reactant)

(deblocking and deacetylation of)  
RN 69124-04-5 HCAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione, 1-(3-O-acetyl-5-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



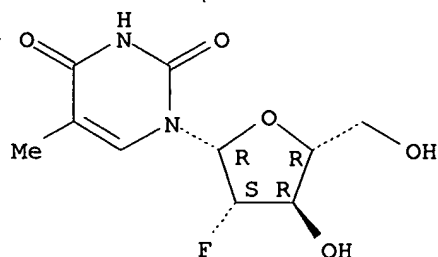
IT 69256-17-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and antiherpes virus activity of)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

L11 ANSWER 74 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1987:60841 HCAPLUS

DOCUMENT NUMBER: 106:60841

TITLE: Comparative efficacy of three 2'-fluoropyrimidine nucleosides and 9-(1,3-dihydroxy-2-propoxymethyl)guanine (BW B759U) against pseudorabies and equine rhinopneumonitis virus infection in vitro and in laboratory animals

AUTHOR(S): Rollinson, Elizabeth A.

CORPORATE SOURCE: Coppers Anim. Health Ltd., Berkhamsted/Hertfordshire, HP4 2QE, UK

SOURCE: Antiviral Res. (1987), 7(1), 25-33

CODEN: ARSRDR; ISSN: 0166-3542

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The 3 2'-fluoropyrimidine nucleosides 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) [69123-90-6], 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouracil (FIAU) [69123-98-4], and 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (FMAU) [69256-17-3], showed high activity in RK13 monolayers against equine rhinopneumonitis virus, (EHV-1), Aujeszky's disease virus (SHV-1, pseudorabies), and infectious bovine rhinotracheitis

virus (1BR, BHV-1). The activity of these compds. was compared with 9-(1,3-dihydroxy-2-propoxymethyl)guanine (BW B759U, DHPG) in 2 lab. animal

disease models: EHV-1-induced hepatitis in hamsters and SHV-1-induced encephalitis in mice. All the compds., provided from 3 to 5 h pre-infection for 5 days, were effective in preventing EHV-1 mortality (at 3-5 mg/kg per day) and in significantly reducing SHV-1 mortality (at 60 mg/kg per day). While FIAU had the greatest activity in vitro, FMAU tended to be more potent in vivo. The reasons for these differences between relative in vitro and in vivo activities are briefly discussed.

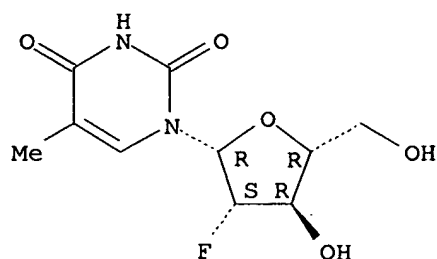
IT **69256-17-3**, 1-(2-Deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antiviral activity of, against pseudorabies and equine rhinopneumonitis virus)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 75 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1987:18982 HCAPLUS

DOCUMENT NUMBER: 106:18982

TITLE: Nucleosides. 139. Synthesis and anticytomegalovirus and antiherpes simplex virus activity of 5'-modified analogs of 2'-fluoroarabinosylpyrimidine nucleosides

AUTHOR(S): Harada, Kazuho; Matulic-Adamic, Jasenka; Price, Richard W.; Schinazi, Raymond F.; Watanabe, Kyoichi A.; Fox, Jack J.

CORPORATE SOURCE: Grad. Sch. Med. Sci., Cornell Univ., New York, NY, 10021, USA

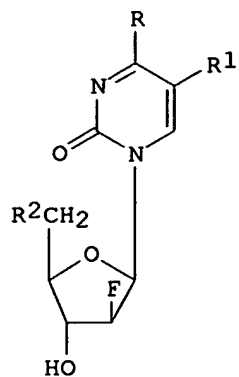
SOURCE: J. Med. Chem. (1987), 30(1), 226-9  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 106:18982

GI



I

AB In order to det. if modification of the 5'-position reduces or abolishes the antiviral activity of the title nucleosides (I, R = NH<sub>2</sub>, OH; R<sub>1</sub> = iodo, Me; R<sub>2</sub> = OH) against human cytomegalovirus (HCMV) and herpes simplex

virus (HSV), I (R<sub>2</sub> = H, SH, NH<sub>2</sub>) were prepd. I (R<sub>2</sub> = H) were prepd. by catalytic hydrogenation of I (R<sub>2</sub> = iodo) followed by reiodination at C-5. I (R<sub>2</sub> = iodo) were inactive against HCMV, indicating that the conversion to 5'-phosphate by cellular enzymes is a requirement for antiviral activity against this virus. Treatment of I (R<sub>2</sub> = O<sub>3</sub>SC<sub>6</sub>H<sub>4</sub>Me-4) with LiN<sub>3</sub> in DMF afforded I (R<sub>2</sub> = N<sub>3</sub>). Catalytic hydrogenation of I (R = OH, R<sub>1</sub> = Me, R<sub>2</sub> = N<sub>3</sub>) afforded I (R = OH, R<sub>1</sub> = Me, R<sub>2</sub> = NH<sub>2</sub>), whereas I (R = NH<sub>2</sub>, R<sub>1</sub> = iodo, R<sub>2</sub> = NH<sub>2</sub>) was obtained by treatment of I (R = NH<sub>2</sub>, R<sub>1</sub> = iodo, R<sub>2</sub> = N<sub>3</sub>) with Ph<sub>3</sub>P in pyridine. I (R<sub>2</sub> = SH) were prepd. by treatment of 5'-O-tosyl-3'-O-acetyl nucleosides with KSAc followed by deacetylation.

I

(R = OH, R<sub>1</sub> = Me, R<sub>2</sub> = NH<sub>2</sub>) was the only compd. that showed good activity against HSV-1 and HSV-2 in vitro. However, this compd. was less potent and had a lower therapeutic index than I (R = R<sub>2</sub> = OH, R<sub>1</sub> = Me).

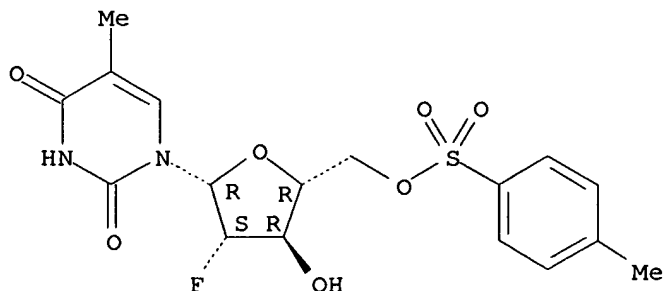
IT 105281-02-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with azide)

RN 105281-02-5 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[(4-methylphenyl)sulfonyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 105281-16-1P

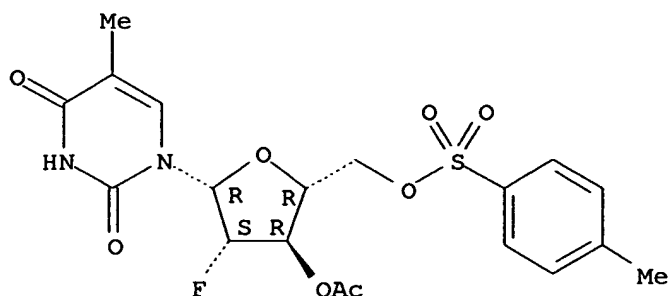
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, with thioacetate)

RN 105281-16-1 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[3-O-acetyl-2-deoxy-2-fluoro-5-O-[(4-methylphenyl)sulfonyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





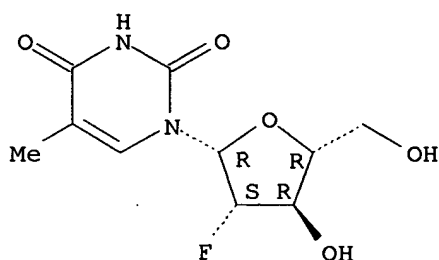
IT 69256-17-3

RL: RCT (Reactant)  
(tosylation of)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 76 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:618182 HCAPLUS

DOCUMENT NUMBER: 105:218182

TITLE: Quantitative determination of antiviral  
**nucleoside** analog in DNA

AUTHOR(S): Chen, Ming S.; Van Nostrand, Mary; Oshana, Scott C.  
CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers Co., Syracuse,  
NY, 13221-4755, USA

SOURCE: Anal. Biochem. (1986), 156(2), 300-4  
CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

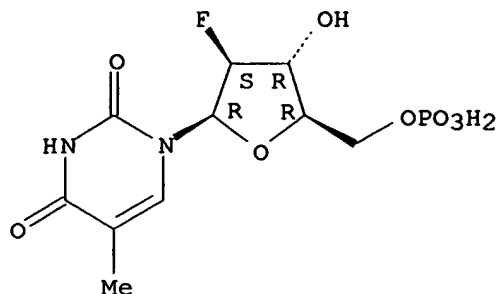
AB A technique for the anal. of the amt. of an antiviral **nucleoside** analog incorporated into DNA utilizing enzymic digestion of DNA, followed by HPLC is described. The cells or tissue samples were treated with perchloric acid to inactivate the nucleases, then digested with pronase in the presence of EDTA. DNA was purified by CsCl centrifugation followed by Sephadex chromatog. and treatment with DNase 1 and venom phosphodiesterase. The deoxyribonucleoside monophosphates and the monophosphate of the **nucleoside** analog liberated from DNA were sepd. and quantitated by HPLC anal. and measurement of radioactivity. This assay is more sensitive, specific, and precise than the detn. of DNA d. shift. It is also applicable for **nucleoside** analogs which do not change the d. of DNA either because of their structure or their very small degree of incorporation.

IT 94344-82-8

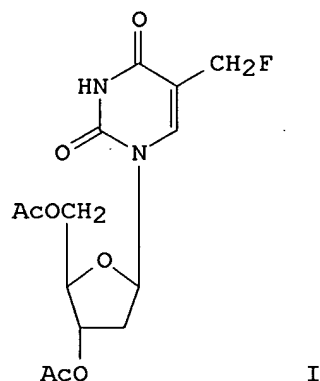
RL: ANT (Analyte); ANST (Analytical study)  
(detn. of, in cells and tissues by HPLC after enzymic digestion)

RN 94344-82-8 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-5-O-phosphono-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

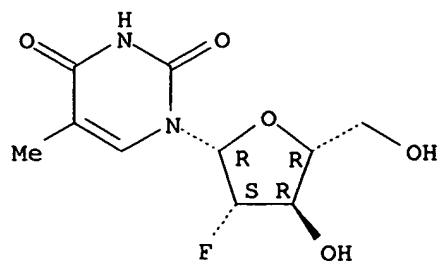


L11 ANSWER 77 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1986:591546 HCAPLUS  
 DOCUMENT NUMBER: 105:191546  
 TITLE: Nucleosides. 138. Synthesis and biological activity of .alpha.-monofluoro- and .alpha.,.alpha.-difluoro-thymine nucleosides  
 AUTHOR(S): Matulic-Adamic, Jasenka; Watanabe, Kyoichi A.; Price, Richard W.  
 CORPORATE SOURCE: Grad. Sch. Med. Sci., Cornell Univ., New York, NY, 10021, USA  
 SOURCE: Chem. Scr. (1986), 26(1), 127-34  
 CODEN: CSRPB9; ISSN: 0004-2056  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 105:191546  
 GI



AB Several title nucleosides were prepd. and their antiherpes activity detd. For example, a soln. of 3',5'-di-O-acetylthymidine in CCl4 was refluxed with Br (irradn. 500 W UV lamp) and the resultant .alpha.-bromothymidine diacetate treated with AgF in MeCN to give .alpha.-fluorothymidine I. Inhibitory concn. of I against HSV-1 and HSV-2 was >100 .mu.M and the toxic concn. was 1000 .mu.M.  
 IT **69256-17-3**  
 RL: RCT (Reactant)  
 (acetylation of)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-

Absolute stereochemistry.



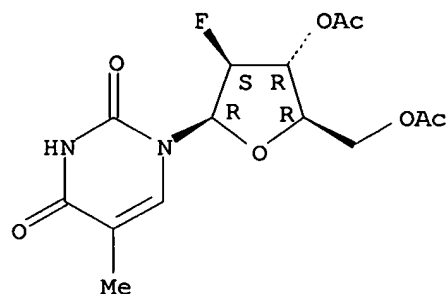
IT 104904-75-8P 104904-80-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and bromination of)

RN 104904-75-8 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(3,5-di-O-acetyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

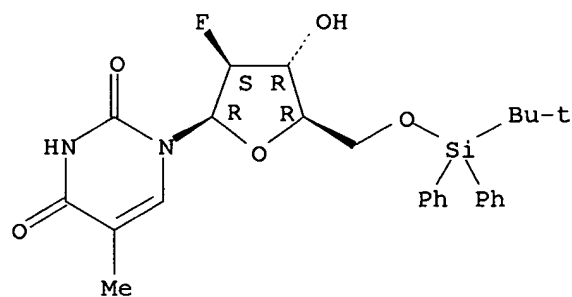


RN 104904-80-5 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-5-O-[(1,1-

dimethylethyl)diphenylsilyl]-2-fluoro-.beta.-D-arabinofuranosyl]-5-methyl-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



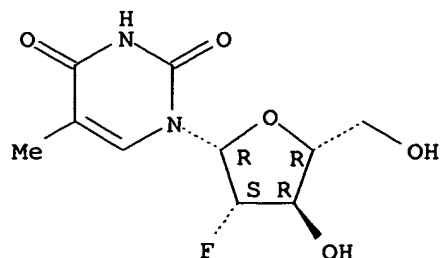
IT 69256-17-3

RL: RCT (Reactant)  
(tert-butyldiphenylsilylation of)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 78 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:490825 HCAPLUS

DOCUMENT NUMBER: 105:90825

TITLE: Susceptibility of varicella-zoster virus to thymidine analogs

AUTHOR(S): Machida, Haruhiko

CORPORATE SOURCE: Res. Lab., Yamasa Shoyu Co., Ltd., Choshi, 288, Japan

SOURCE: Biken J. (1986), 29(1), 1-6

CODEN: BKNJA5; ISSN: 0006-2324

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ten strains of varicella-zoster virus (VZS) were tested for susceptibility

to 17 nucleoside analogs by a plaque redn. assay using human embryonic lung fibroblast cells. The compds. employed were 5-substituted arabinosyluracils and 2'-deoxyuridines, 2'-fluoro-arabinosylpyrimidines (F-araPyr) and acyclovir [59277-89-3]. In terms of the 50% plaque redn. dose (PD50), 4- to 40-fold difference were found between the 10 strains of

VZV in susceptibilities to each compd. VZV was highly susceptible to 5-halogenovinyl-arabinosyluracils (XV-araUs); the PD50 values of these compds. were less than 0.001 .mu.g/mL. VZV was much more susceptible than

either HSV type 1 or type 2 to 5-ethyl-2'-deoxyuridine [15176-29-1], 5-ethylarabinosyluracil [70020-72-3], and acyclovir.

IT 69256-17-3

RL: BIOL (Biological study)

(varicella-zoster virus susceptibility to)

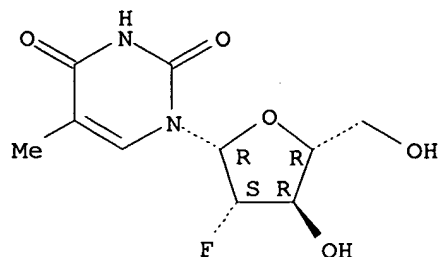
RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-

5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 79 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:472131 HCAPLUS

DOCUMENT NUMBER: 105:72131

TITLE: Enzymology and pathogenicity in mice of a herpes simplex virus type 1 mutant resistant to

2'-fluoro-2'-deoxy-1-.beta.-D-arabinofuranosyl-5-iodocytosine  
AUTHOR(S): Colacino, Joseph; Brownridge, Elizabeth; Greenberg, Nancy; Lopez, Carlos  
CORPORATE SOURCE: Lab. Herpesvirus Infect., Mem. Sloan Kettering Cancer Cent., New York, NY, 10021, USA  
SOURCE: Antimicrob. Agents Chemother. (1986), 29(5), 877-82  
CODEN: AMACQ; ISSN: 0066-4804  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The deoxypyrimidine **nucleoside** analog 2-fluoro-2'-deoxy-1-.beta.-D-arabinofuranosyl-5-iodocytosine (FIAC) [69123-90-6] is a potent and selective inhibitor of herpes simplex virus type I in vitro. Isopycnog. anal. demonstrated that 1 .mu.M FIAC inhibited herpes simplex virus DNA replication by more than 95% but inhibited cellular DNA replication by only 32%. Mutant herpes simplex virus type 1 selected resistant to FIAC displayed linked resistance to other **nucleoside** analogs, including arabinosylthymine [605-23-2] and acyclovir [59277-89-3]. Lysates derived from Vero cells infected with FIAC-resistant virus showed markedly lower levels of thymidine kinase [9002-06-6] activity and were unable to phosphorylate selectively arabinosylthymine or FIAC, in

contrast to lysates from the cells infected with wild-type herpes simplex virus type 1. Drug-resistant virus displayed a 6,000-fold decrease in pathogenicity when inoculated i.p. into genetically susceptible A/J mice. These results indicate that resistance to deoxypyrimidine **nucleoside** analogs is due, at least in part, to alterations in viral thymidine kinase and is accompanied by decreased pathogenicity in vivo.

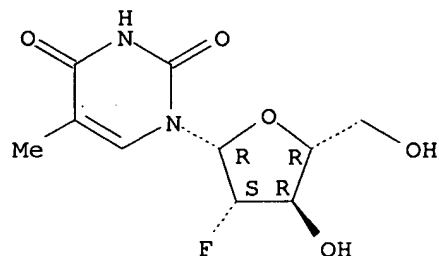
IT 69256-17-3

RL: BIOL (Biological study)  
(herpes virus resistant to fluorodeoxyarabinofuranosyliodocytosine sensitivity to)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

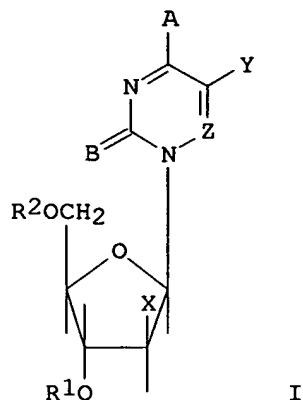
Absolute stereochemistry.



L11 ANSWER 80 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1986:180200 HCAPLUS  
DOCUMENT NUMBER: 104:180200  
TITLE: Treatment of hepatitis with pyrimidine nucleosides  
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA  
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 60252418	A2	19851213	JP 1985-44479	19850306
AU 8539534	A1	19850912	AU 1985-39534	19850305
AU 575918	B2	19880811		
HU 39189	A2	19860828	HU 1985-827	19850305
HU 198393	B	19891030		
US 4666892	A	19870519	US 1986-828569	19860210
PRIORITY APPLN. INFO.:			US 1984-586729	19840306
GI				



AB 5-Substituted 1-(2'-deoxy-2'-substituted-.beta.-D-arabinofuranosyl)pyrimidines I, where A = OR<sub>3</sub>, SR<sub>3</sub>, NR<sub>3</sub>R<sub>4</sub>, or acylamido; R<sub>3</sub>, R<sub>4</sub> = H, C1-7 alkyl, aralkyl, or aryl; B = O or S; X = halo, alkylsulfonyl, or arylsulfonyl; Y = halo, amino, alkyl, etc.; Z = C or N; R<sub>1</sub>, R<sub>2</sub> = H, acyl, or aroyl, are effective in treatment of hepatitis B virus infection. The efficacies of several compds. such as 2'-fluoro-2'-deoxyarabinosyl-5-iodocytosine were shown in patients.

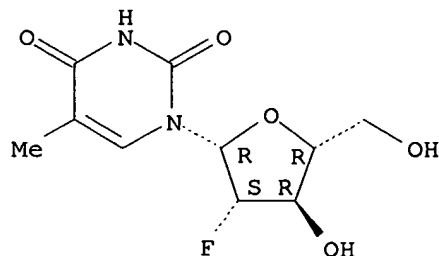
IT 69256-17-3

RL: BIOL (Biological study)  
(hepatitis treatment with)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d 111 82-90 ibib abs hitstr

L11 ANSWER 82 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:179765 HCAPLUS

DOCUMENT NUMBER: 104:179765

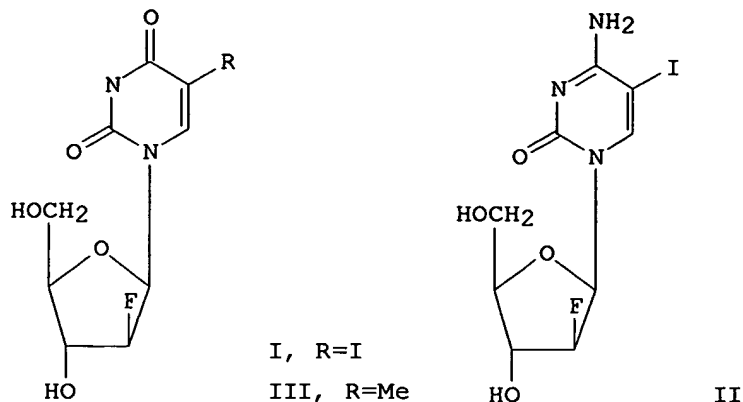
TITLE: Preclinical investigations of FIAU, an anti-herpes agent

AUTHOR(S): McLaren, C.; Chen, M. S.; Barbhaiya, R. H.; Buroker,

CORPORATE SOURCE:  
SOURCE:

R. A.; Oleson, F. B.  
Bristol-Myers Co., Syracuse, NY, 13221-4755, USA  
Int. Congr. Ser. - Excerpta Med. (1985), 667 (Herpes  
Viruses Virus Chemother.), 57-61  
CODEN: EXMDA4; ISSN: 0531-5131  
Journal  
English

DOCUMENT TYPE:  
LANGUAGE:  
GI



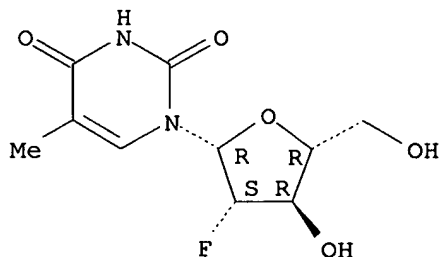
AB The pharmacol. of FIAU (I) [69123-98-4] as an anti-herpes agent is described in relation to that of FIAC (II) [69123-90-6] and FMAU (III)

[  
69256-17-3]. The mechanism of action of I is dependent on selective inhibition of viral thymidine kinase [9002-06-6]. The I monophosphate [99891-31-3] and III monophosphate [94344-82-8] had better affinities for cellular thymidylate kinase [9014-43-1] than for herpes simplex virus thymidine/thymidylate kinases. However, II monophosphate [99876-43-4] had poor affinities for either the cellular or herpes simplex virus enzymes. In cells exposed to 14C-labeled II, I monophosphate was the major metabolite, indicating that II is converted to the more active agent, I. I appeared to have good activity, but it had cardiotoxic and myelosuppressive activities.

IT 69256-17-3  
RL: BIOL (Biological study)  
(herpes virus inhibition by, thymidine kinase inhibition in, toxicity in relation to)

RN 69256-17-3 HCAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



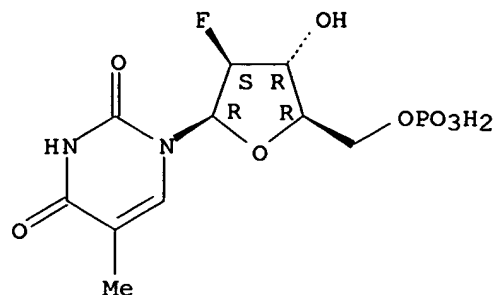
IT 94344-82-8  
RL: BIOL (Biological study)

(thymidylate kinase inhibition by, herpes virus inhibition in relation to)

RN 94344-82-8 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-5-O-phosphono-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 83 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1986:81578 HCAPLUS

DOCUMENT NUMBER: 104:81578

TITLE: Activities of 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine and its metabolites against herpes simplex virus types 1 and 2 in cell culture and in mice infected intracerebrally with herpes simplex virus type 2

AUTHOR(S): Schinazi, Raymond F.; Fox, Jack J.; Watanabe, Kyoichi A.; Nahmias, Andre J.

CORPORATE SOURCE: Veterans Adm. Med. Cent., Atlanta, GA, 30303, USA

SOURCE: Antimicrob. Agents Chemother. (1986), 29(1), 77-84  
CODEN: AMACQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As measured by plaque and yield redn. assays, several metabolites of 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) were highly active against herpes simplex virus types 1 and 2. These metabolites included the 2'-deoxy-2'-fluoroarabinosyl derivs. of 5-iodouracil, cytosine, uracil, and thymine. In mice inoculated intracerebrally with herpes simplex virus type 2, the relative order of potency of these compds. and known antiviral drugs were as follows:  
2'-fluoro-5-methylarabinosyluracil (FMAU) [69256-17-3] .mchgt.  
2'-fluoro-5-iodoarabinosylcytosine (FIAC) [69123-90-6] .apprxeq.  
2'-fluoro-5-iodoarabinosyluracil (FIAU) [69123-98-4] > acyclovir .apprxeq. vidarabine .mchgt. 2'-fluoroarabinosylcytosine (FAC) [56632-83-8] .apprxeq. 2'-fluoroarabinosyluracil (FAU) [69123-94-0].

One

of the main metabolites of FMAU,  
2'-fluoro-5-hydroxymethylarabinosyluracil [94817-51-3], was essentially inactive in vivo. FIAC-, FIAU-, FMAU-, FAC-, and FAU-resistant herpes simplex virus variants prepd. in cell culture were found to be (i) devoid of viral thymidine kinase [9002-06-6], (ii) cross-resistant to one another and resistant to drugs requiring viral thymidine kinase for activation, and (iii) sensitive to vidarabine or phosphonoformate. These results indicate that FIAC, FIAU, and FMAU require the virally encoded thymidine kinase for activation and suggest that the antiviral activity of FAU and FAC in cell cultures is also mediated by this enzyme. The interaction of the fluoroarabinosylpyrimidine nucleosides with herpes simplex virus thymidine

kinase in a cell-free system is also described.

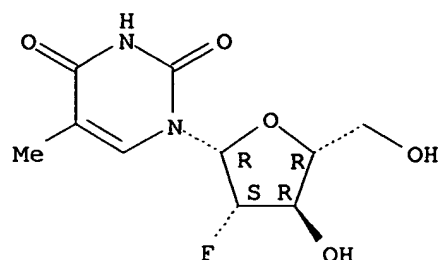
IT 69256-17-3

RL: BIOL (Biological study)



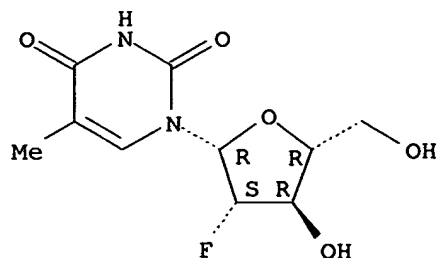
(herpes simplex virus type 2 inhibition by)  
RN 69256-17-3 HCAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



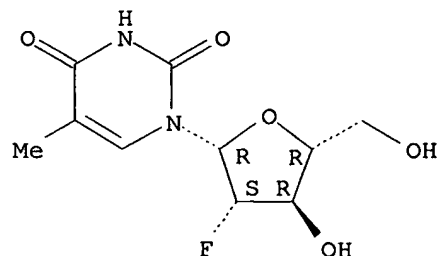
L11 ANSWER 84 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1986:81562 HCAPLUS  
DOCUMENT NUMBER: 104:81562  
TITLE: Selective inhibition of the proliferation of herpes  
simplex virus type 1 thymidine kinase  
gene-transformed .  
murine mammary FM3A carcinoma cells by  
(E)-5-(2-bromovinyl)-2'-deoxyuridine and related  
compounds  
AUTHOR(S): Balzarini, J.; De Clercq, E.; Ayusawa, D.; Shimizu,  
K.; Seno, T.  
CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain,  
B-3000, Belg.  
SOURCE: Nucleic Acids Symp. Ser. (1985), 16(Symp. Nucleic  
Acids Chem., 13th), 283-6  
CODEN: NACSD8; ISSN: 0261-3166  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Mouse mammary carcinoma FM3A cells deficient in thymidine kinase  
[9002-06-6] were transformed by a cloned gene for herpes simplex virus  
type 1 thymidine kinase. Among several antiherpetic **nucleoside**  
analog, (E)-5-(2-bromovinyl)-2'-deoxyuridine [69304-47-8],  
(E)-5-(2-iodovinyl)-2'-deoxyuridine [69304-48-9], and  
(E)-5-(2-bromovinyl)-2'-deoxycytidine [74131-09-2] inhibited the growth  
of the transformed cells at concns. 5000- to 20000-fold lower than those  
required to inhibit the growth of their corresponding wild-type cells.  
The selective inhibitory action of these compds. was due to a specific  
phosphorylation by the viral thymidine kinase. From the transformed  
cells, thymidine-auxotrophic mutants that are deficient in thymidylate  
synthase were isolated. These mutant cell lines should prove useful in  
elucidating the mechanism of action of the antiherpetic **nucleoside**  
analogs.  
IT 69256-17-3  
RL: BIOL (Biological study)  
(herpes simplex virus type 1 thymidine kinase gene-transformed mammary  
carcinoma cell growth inhibition by)  
RN 69256-17-3 HCAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 85 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1986:45371 HCAPLUS  
 DOCUMENT NUMBER: 104:45371  
 TITLE: Effects of **nucleoside** analogs in inhibition of Epstein-Barr virus  
 AUTHOR(S): Lin, J. C.; Nelson, D. J.; Lambe, C. U.; Choi, E. I.; Pagano, J. S.  
 CORPORATE SOURCE: Lineberger Cancer Res. Cent., Univ. North Carolina, Chapel Hill, NC, 27514, USA  
 SOURCE: Int. Congr. Ser. - Excerpta Med. (1985), 667(Herpes Viruses Virus Chemother.), 225-7  
 CODEN: EXMDA4; ISSN: 0531-5131  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The relative antiviral potency of several **nucleoside** analogs against Epstein-Barr virus infection in P3HR-1 cells was 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (I) [69123-90-6] = 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouracil (II) [69123-98-4] > 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-thymine (III) [69256-17-3] > BW B759U (IV) [82410-32-0] > E-5-(2-bromovinyl)-2'-deoxyuridine (V) [69304-47-8] > acyclovir (VI); the relative therapeutic efficacy (ratio of cytotoxicity to antiviral potency) was V > IV > I > VI > II > III. IV was rapidly and markedly phosphorylated by virus-infected Raji cells; this effect was 100-fold greater than for VI. The results are discussed with respect to the prolonged inhibitory action of the **nucleoside** analogs against Epstein-Barr virus replication.  
 IT 69256-17-3  
 RL: BIOL (Biological study)  
 (Epstein-Barr virus infection inhibition by)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 86 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1986:45345 HCAPLUS

L11 ANSWER 87 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1986:14570 HCAPLUS  
DOCUMENT NUMBER: 104:14570  
TITLE: Human cytomegalovirus-induced DNA polymerase and its interaction with the triphosphates of 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil, -5-iodocytosine, and -5-methylcytosine  
AUTHOR(S): Mar, Eng Chun; Chiou, Jwo Farn; Cheng, Yung Chi; Huang, Eng Shang  
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA  
SOURCE: J. Virol. (1985), 56(3), 846-51  
CODEN: JOVIAM; ISSN: 0022-538X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Human cytomegalovirus-induced DNA polymerase [9012-90-2] and cellular DNA

polymerase .alpha. were purified by successive chromatog. on DEAE-cellulose, phosphocellulose, heparin agarose, and single-stranded DNA

agarose columns. The purified virus-induced DNA polymerase was resolved to 2 polypeptides corresponding to mol. wts. of 140,000 and 58,000, as analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Virus-induced DNA polymerase and cellular .alpha. polymerase were examd. for their sensitivities to the triphosphates of 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (FMAUTP) [69256-17-3], -5-iodocytosine (FIACTP) [69123-90-6], and -5-methylcytosine (FMACTP) [78636-53-0]. The inhibitive effects of these triphosphates on the DNA polymerases were competitive with regard to the natural substrates; thus FMAUTP completes with dTTP [365-08-2], and FIACTP and FMACTP complete with dCTP [2056-98-6]. The inhibition consts. (Ki) for FMAUTP, FIACTP, and FMACTP of virus-induced DNA polymerase are 0.06, 0.30, and 0.47

.mu.M, resp. Cellular DNA polymerase .alpha. is much less sensitive to these inhibitors, and its Ki values for FMAUTP, FIACTP, and FMACTP are 0.45, 3.10, and 2.90 .mu.M, resp. In addn., human cytomegalovirus-induced DNA polymerase, but not cellular DNA polymerase .alpha., can utilize these analog triphosphates as alternate substrates for their corresponding natural deoxyribonucleoside triphosphates in in vitro DNA synthesis.

IT 69256-17-3

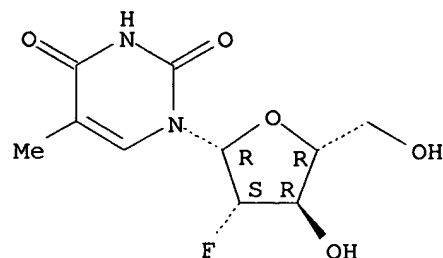
RL: BIOL (Biological study)

(DNA polymerase of cell and induced by human cytomegalovirus response to, antiviral mechanism in relation to)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

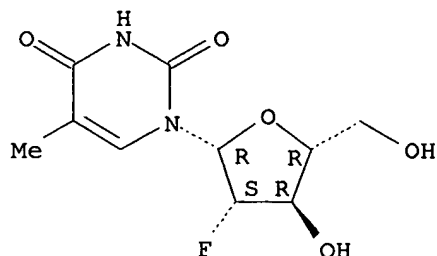
Absolute stereochemistry.



L11 ANSWER 88 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1985:605545 HCAPLUS  
DOCUMENT NUMBER: 103:205545  
TITLE: Ab initio studies of the antiviral drug

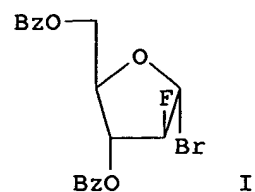
9-(1,3-dihydroxy-2-propoxymethyl)guanine, acyclovir, and two 2'-fluoropyrimidine nucleosides  
 AUTHOR(S): Smee, Donald F.; Campbell, Nancy L.; Matthews, Thomas R.  
 CORPORATE SOURCE: Syntex Res., Mountain View, CA, 94043, USA  
 SOURCE: Antiviral Res. (1985), 5(5), 259-67  
 CODEN: ARSRDR; ISSN: 0166-3542  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 9-(1,3-Dihydroxy-2-propoxymethyl)guanine (DHPG) [82410-32-0], was evaluated in cell culture and in animals for its inhibitory effect on herpes simplex viruses. Compds. used for comparison included acyclovir [59277-89-3], 2'-fluoro-2'-deoxy-5-iodoarabinofuranosylcytosine (FIAC) [69123-90-6], and 2'-fluoro-2'-deoxy-5-methylarabinofuranosyluracil (FMAU) [69256-17-3]. In plaque-redn. assays DHPG, acyclovir, FIAC, and FMAU were inhibitory to 6 herpes types 1 and 2 virus strains at concns. of 0.2-2.4 .mu.M. These concns. were much lower than those required to inhibit Vero cell proliferation. In guinea pig vaginal infections, DHPG provided significantly greater inhibition of herpetic lesions than did acyclovir. In a herpes type 2 infection model in mice, DHPG, and FMAU were active at 5 mg/kg, whereas acyclovir and FIAC showed no statistically significant effect at 80 mg/kg. In a herpes type 1 encephalitis model, DHPG and FMAU were active at doses <10 mg/kg, with FMAU being about 4 times more potent than DHPG in that model.  
 IT 69256-17-3  
 RL: BIOL (Biological study)  
 (antiherpes virus activity of, (dihydroxypropoxymethyl)guanine in comparison with)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 90 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:523851 HCAPLUS  
 DOCUMENT NUMBER: 103:123851  
 TITLE: Fluorocarbohydrates in synthesis. An efficient synthesis of 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodouracil (.beta.-FIAU) and 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)thymine (.beta.-FMAU)  
 AUTHOR(S): Tann, Chou H.; Brodfuehrer, Paul R.; Brundidge, Steven  
 CORPORATE SOURCE: P.; Sapino, Chester, Jr.; Howell, Henry G. Pharm. Res. Dev. Div., Bristol-Myers, Syracuse, NY, 13221-4755, USA  
 SOURCE: J. Org. Chem. (1985), 50(19), 3644-7  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DOCUMENT TYPE: Journal

LANGUAGE: English  
OTHER SOURCE(S): CASREACT 103:123851  
GI



AB A 4-step, highly efficient synthesis of .beta.-FIAU and .beta.-FMAU is reported. 2-Deoxy-2-fluoro-1,3,5-tri-O-benzoyl-.alpha.-D-arabinofuranose was prepd. from 1,3,5-tri-O-benzoyl-.alpha.-D-ribofuranose, by fluorination of the corresponding 2-O-(imidazolylsulfonyl) deriv. in 63% yield. The use of anomerically pure bromide I for coupling to the **nucleoside** base results in higher yields of the desired .beta.-nucleosides.

IT 97614-47-6P 97614-48-7P

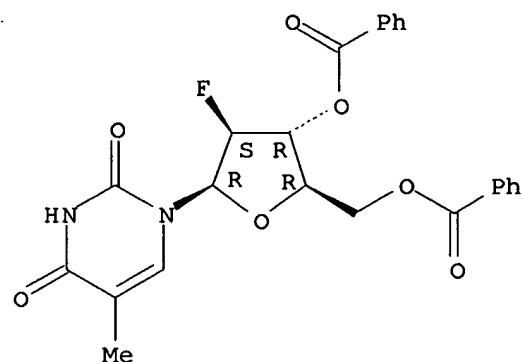
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and debenzoylation of)

RN 97614-47-6 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(3,5-di-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

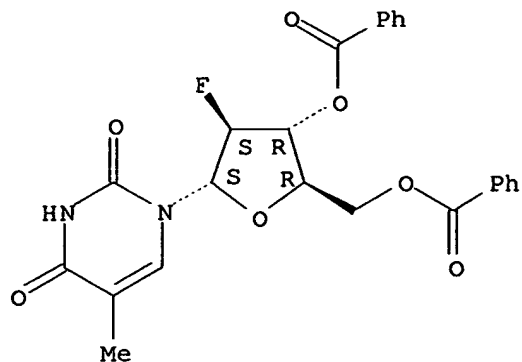


RN 97614-48-7 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

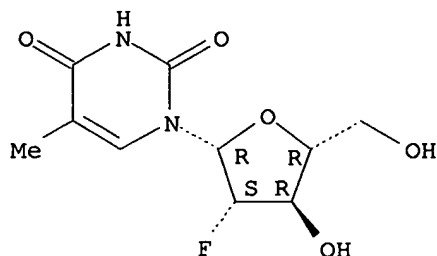
1-(3,5-di-O-benzoyl-2-deoxy-2-fluoro-.alpha.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



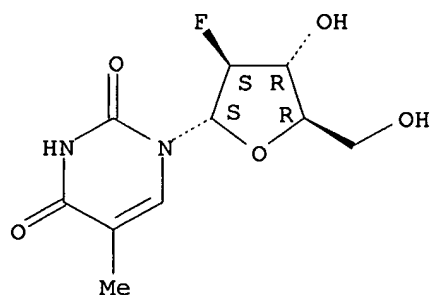
IT 69256-17-3P 97672-34-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 97672-34-9 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-.alpha.-D-  
 arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

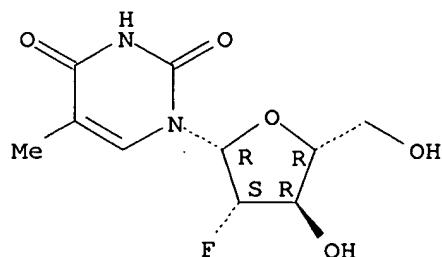


=> d l11 91-101 ibib abs hitstr

L11 ANSWER 91 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:481377 HCAPLUS  
 DOCUMENT NUMBER: 103:81377  
 TITLE: Murine mammary FM3A carcinoma cells transformed with  
 the herpes simplex virus type 1 thymidine kinase gene  
 are highly sensitive to the growth-inhibitory

and properties of (E)-5-(2-bromovinyl)-2'-deoxyuridine  
 related compounds  
 AUTHOR(S): Balzarini, J.; De Clercq, E.; Ayusawa, D.; Seno, T.  
 CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain,  
 B-3000, Belg.  
 SOURCE: FEBS Lett. (1985), 185(1), 95-100  
 CODEN: FEBLAL; ISSN: 0014-5793  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Murine mammary carcinoma (FM3A TK-/HSV-1 TK+) cells, which are thymidine  
 kinase (TK) [9002-06-6]-deficient but have been transformed with the  
 herpes simplex virus type 1 (HSV-1) TK gene, are inhibited in their  
 growth by (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU) [69304-47-8],  
 (E)-5-(2-iodovinyl)-2'-deoxyuridine [69304-48-9], and  
 (E)-5-(2-bromovinyl)-  
 2'-deoxycytidine [74131-09-2] at 0.5, 0.5 and 0.8 ng/mL, resp. (i.e., a  
 concn. 5000-20,000-fold lower than that required to inhibit the growth of  
 the corresponding wild-type FM3A/0 cells). Hence, transformation of  
 tumor cells with the HSV-1 TK gene makes them particularly sensitive to the  
 cytostatic action of BVDU and related compds.  
 IT 69256-17-3  
 RL: PRP (Properties)  
 (cytotoxicity of, to herpes virus-transformed carcinoma cell,  
 thymidine kinase in relation to)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 92 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:447858 HCAPLUS  
 DOCUMENT NUMBER: 103:47858  
 TITLE: Comparative efficacy and selectivity of some  
 nucleoside analogs against Epstein-Barr virus  
 AUTHOR(S): Lin, Jung Chung; Smith, M. Carolyn; Pagano, Joseph S.  
 CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC,  
 27514, USA  
 SOURCE: Antimicrob. Agents Chemother. (1985), 27(6), 971-3  
 CODEN: AMACQ; ISSN: 0066-4804  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of (2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine  
 (FIAC) [69123-90-6], 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-  
 methyluridine (FMAU) [69256-17-3], 1-(2-deoxy-2-fluoro-.beta.-D-  
 arabinofuranosyl)-5-iodouridine (FIAU) [69123-98-4],  
 (E)-5-(2-bromovinyl)-  
 2'-deoxyuridine (BVdU) [69304-47-8], and 9-(1,3-dihydroxy-2-  
 propoxymethyl)guanine (DHPG or BW B759U) [82410-32-0] on the replication

of Epstein-Barr virus (EBV) in vitro were evaluated and compared with that of acyclovir (ACV). The relative potencies of these drugs, on the basis of anti-EBV activity, were: FIAC = FIAU > FMAU > DHPG > BVdU > ACV; on the basis of the therapeutic index they were: BVdU > DHPG > FIAC > ACV > FIAU > FMAU. Differential inhibition of EBV-assocd. polypeptides by these drugs was obsd.

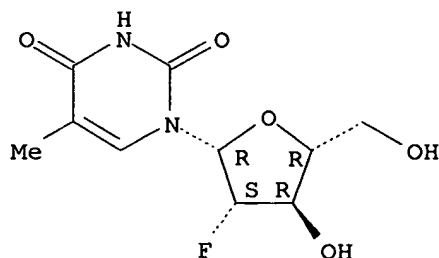
IT 69256-17-3

RL: BIOL (Biological study)  
(Epstein-Barr virus inhibition by)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 93 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:416283 HCAPLUS

DOCUMENT NUMBER: 103:16283

TITLE: Incorporation of 5-substituted pyrimidine  
**nucleoside** analogs into DNA of a thymidylate  
synthetase-deficient murine FM3A carcinoma cell line  
AUTHOR(S): Balzarini, Jan; De Clercq, Erik; Ayusawa, Dai; Seno,  
Takeshi

CORPORATE SOURCE: Rega Inst. Med. Res., Univ. Leuven, Louvain, B-3000,  
Belg.

SOURCE: Methods Find. Exp. Clin. Pharmacol. (1985), 7(1),  
19-28

CODEN: MFEPDX; ISSN: 0379-0355

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A thymidylate (dTMP) synthetase [9031-61-2]-deficient murine mammary carcinoma cell line (FM3A/T5) which is auxotrophic for thymidine (dThd) was developed as a system with which to screen pyrimidine **nucleoside** analogs for their ability to sustain cell growth and, apparently, be incorporated into host-cell DNA. A no. of 5-substituted derivs. of 2'-deoxyuridine (dUrd) and 2'-deoxycytidine (dCyd) were found to stimulate growth, the dCyd derivs. apparently being deaminated to their

dUrd analogs before incorporation into DNA. None of the 5-substituted derivs. of 1-.beta.-D-arabinofuranosyluracil or 1-.beta.-D-arabinofuranosylcytosine were growth-stimulating.

IT 69256-17-3

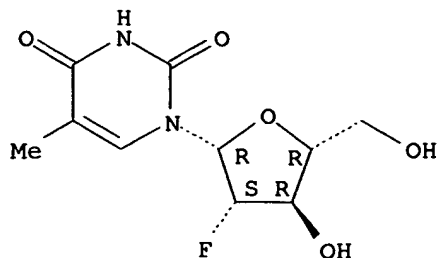
RL: PROC (Process)  
(DNA incorporation of, in thymidylate synthetase-deficient murine  
mammary carcinoma cell line)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

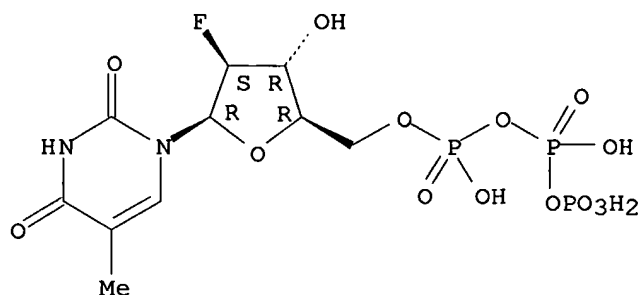
Absolute stereochemistry.





L11 ANSWER 94 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:201003 HCAPLUS  
 DOCUMENT NUMBER: 102:201003  
 TITLE: Interaction of Epstein-Barr virus DNA polymerase and 5'-triphosphates of several antiviral nucleoside analogs  
 AUTHOR(S): Chiou, Jwo Farn; Cheng, Yung Chi  
 CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA  
 SOURCE: Antimicrob. Agents Chemother. (1985), 27(3), 416-18  
 CODEN: AMACQ; ISSN: 0066-4804  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The 5'-triphosphates of 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil, 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine, 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methylcytosine, 9-[(2-hydroxyethoxy)methyl]guanine, and 9-(1,3-dihydroxy-2-propoxymethyl)guanine had lower  $K_i$  values for Epstein-Barr virus DNA polymerase than has been reported elsewhere for host DNA polymerase. Inhibition of DNA elongation by these analogs ranged from moderate to strong, suggesting that preferential incorporation of these analogs into DNA by virus DNA polymerase may contribute to antiviral selectivity.  
 IT 79551-89-6  
 RL: BIOL (Biological study)  
 (Epstein-Barr virus DNA polymerase interaction with)  
 RN 79551-89-6 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-[hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



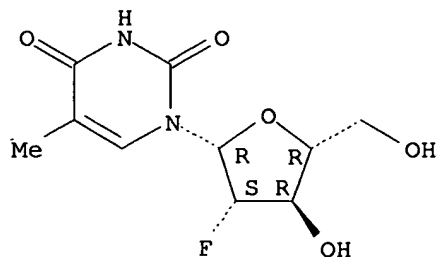
L11 ANSWER 95 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:178764 HCAPLUS  
 DOCUMENT NUMBER: 102:178764

TITLE: Treatment of genital herpes simplex virus infections  
in guinea pigs  
AUTHOR(S): Kern, Earl R.  
CORPORATE SOURCE: Sch. Med., Univ. Utah, Salt Lake City, UT, 84132, USA  
SOURCE: UCLA Symp. Mol. Cell. Biol., New Ser. (1984),  
21(Herpesvirus), 617-36  
CODEN: USMBD6; ISSN: 0735-9543  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Intravaginal inoculation of guinea pigs with herpes simplex virus type 2 provides an excellent model for genital herpes in humans. The infection is characterized by local viral replication in the vaginal tract followed by the appearance of vesicular lesions on external genital skin. After recovery from the primary infection, spontaneous recurrent lesions appear on the external genitalia. Oral treatment with acyclovir [59277-89-3], 2'-deoxy-2'-fluoro-5-iodoarabinosylcytosin [69123-90-6], 2'-fluoro-5-iodoarabinosyluracil [69123-98-4], 2'-fluoro-5-methylarabinosyluracil [69256-17-3], 9-(1,3-dihydroxy-2'-propoxymethyl)guanine [82410-32-0], and i.m. treatment with recombinant human interferon-.alpha.A all reduced the severity of the primary infection. All compds. administered during recurrent disease also reduced the frequency of recurrent episodes, however, the frequency of recurrences returned to the level of controls when therapy was terminated.

IT 69256-17-3  
RL: BIOL (Biological study)  
(genital herpes simplex virus infection treatment with)  
RN 69256-17-3 HCAPLUS  
CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 96 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1985:146012 HCAPLUS  
DOCUMENT NUMBER: 102:146012  
TITLE: Drug resistant and hypersensitive herpes simplex  
virus  
mutants: isolation and application to dissection of  
the pol locus  
AUTHOR(S): Coen, Donald M.; Chiou, Henry C.; Fleming, H. Edward,  
Jr.; Leslie, Laurel K.; Retondo, Margaret J.  
CORPORATE SOURCE: Dep. Pharmacol., Harvard Med. Sch., Boston, MA,  
02115,  
USA  
SOURCE: UCLA Symp. Mol. Cell. Biol., New Ser. (1984),  
21(Herpesvirus), 373-85  
CODEN: USMBD6; ISSN: 0735-9543  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Herpes simplex virus mutants resistant to antiviral drugs and aphidicolin are readily isolated in a single-step selection procedure. However, it

was found that mutants resistant to one drug are often not substantially cross-resistant to others suggesting possible solns. to potential clin. resistance. Repeated plaque purifn. has proven essential for such analyses. Previous studies have identified PAA-, ACG-, and araA-resistance mutations in the DNA polymerase (pol) locus. Mutations conferring hypersensitivity to araA, PAA, FMAU, FIAU, BVdU, 2'NDG, and aphidicolin (Aph) were identified and several of these were mapped to the pol locus. The existence of either type of mutation in the pol locus implies that polymerase is a target for the drugs or otherwise mediates drug-sensitivity. Addnl., cross-resistance patterns of the mutants suggest that polymerases capable of discriminating against one nucleoside analog are incapable of discriminating against closely related compds. Mutations conferring altered sensitivity to the same

drug

map at different locations in the pol locus. Anal. of these mutations should aid in the functional dissection of the polymerase.

IT 69256-17-3

RL: BIOL (Biological study)

(resistance to, of herpes simplex virus, DNA polymerase gene in relation to)

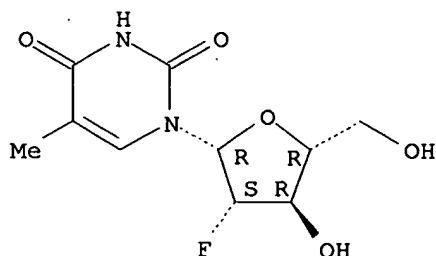
RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-

5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 97 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:113894 HCAPLUS  
 DOCUMENT NUMBER: 102:113894  
 TITLE: Nucleosides  
 INVENTOR(S): Hertel, Larry Wayne  
 PATENT ASSIGNEE(S): Lilly, Eli, and Co. , USA  
 SOURCE: Brit. UK Pat. Appl., 17 pp.  
 CODEN: BAXXDU  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

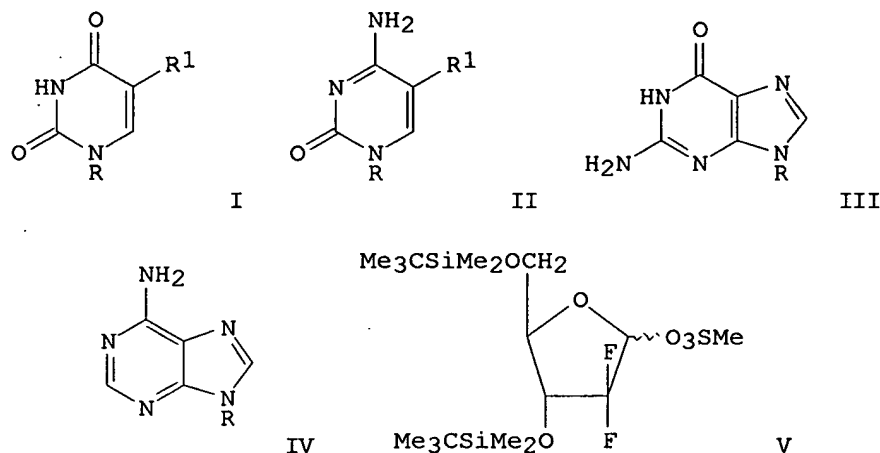
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2136425	A1	19840919	GB 1984-5805	19840306
GB 2136425	B2	19870513		
US 4526988	A	19850702	US 1983-473883	19830310
DK 8401144	A	19840911	DK 1984-1144	19840228
DK 162529	B	19911111		
DK 162529	C	19920330		
RO 89963	B3	19860930	RO 1984-113763	19840229
ZA 8401605	A	19851030	ZA 1984-1605	19840302
CA 1218647	A1	19870303	CA 1984-448698	19840302
IL 71143	A1	19880731	IL 1984-71143	19840304
IL 80463	A1	19880731	IL 1984-80463	19840304
FI 8400890	A	19840911	FI 1984-890	19840306

FI 77870	B	19890131		
FI 77870	C	19890510		
EP 122707	A1	19841024	EP 1984-301463	19840306
EP 122707	B1	19870916		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 29726	E	19871015	AT 1984-301463	19840306
AU 8425374	A1	19840913	AU 1984-25374	19840307
AU 565856	B2	19871001		
ES 530364	A1	19851201	ES 1984-530364	19840307
SU 1442076	A3	19881130	SU 1984-3710351	19840307
DD 216468	A5	19841212	DD 1984-260703	19840308
CS 246075	B2	19861016	CS 1984-1667	19840308
JP 59175498	A2	19841004	JP 1984-46387	19840309
JP 05042438	B4	19930628		
HU 33813	O	19841228	HU 1984-963	19840309
HU 193893	B	19871228		
PL 142437	B1	19871031	PL 1984-246601	19840309
GB 2172287	A1	19860917	GB 1986-10648	19860501
GB 2172287	B2	19870520		
CA 1223869	A2	19870707	CA 1986-509195	19860514
DK 9001905	A	19900810	DK 1990-1905	19900810
DK 170647	B1	19951120		
JP 06009602	A2	19940118	JP 1993-4752	19930114
JP 06102655	B4	19941214		

PRIORITY APPLN. INFO.:

US 1983-473883 19830310  
CA 1984-448698 19840302  
IL 1984-71143 19840304  
EP 1984-301463 19840306  
GB 1984-5805 19840306

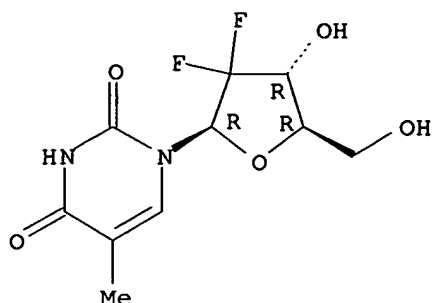
GI



AB Difluoro nucleosides I-IV [R = 2-deoxy-2,2-difluoro- $\alpha$ -( $\beta$ )-D-pentofuranosyl; R1 = H, Me, halogen, CH:CHR2; R2 = Cl, Br, iodo] were prepd. Thus, 4-formyl-2,2-dimethyldioxolane, prepd. from D-glyceraldehyde, was condensed with BrCF2CO2Et to give a 3:1 mixt. of Et (3R)- and (3S)-2,2-difluoro-3-hydroxy-3-(2,2-dimethyldioxolan-4-yl)propionate. The 3R-isomer was hydrolyzed to give the ribonolactone, which was tert-butyldimethylsilylated, reduced with (Me2CHCH2)2AlH, and mesylated to give ribose deriv. V. V was condensed with 5-methyl-2,4-bis(trimethylsiloxy)pyrimidine to give the silylated nucleoside which was desilylated with HBr to give I [R = 2-deoxy-2,2-difluoro- $\alpha$ -( $\beta$ )-ribofuranosyl, R1 = Me; VI].  $\beta$ -VI at 0.31  $\mu$ g/mL inhibited the growth of herpes simplex virus, type 1 by 50% compared with 7.6 and 1.74  $\mu$ g/mL for Ara-A and Acyclovir,

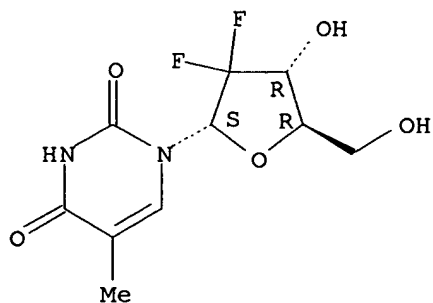
resp.  
 IT 95058-80-3P 95058-84-7P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. and virucidal activity of)  
 RN 95058-80-3 HCAPLUS  
 CN Thymidine, 2',2'-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 95058-84-7 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2,2-difluoro-.alpha.-D-erythro-pentofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 98 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1985:109059 HCAPLUS  
 DOCUMENT NUMBER: 102:109059  
 TITLE: Quantitative autoradiographic mapping of focal herpes simplex virus encephalitis using a radiolabeled antiviral drug  
 INVENTOR(S): Price, Richard  
 PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA  
 SOURCE: U.S., 4 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4489052	A	19841218	US 1982-418156	19820915

AB A diagnostic, noninvasive test for herpes simplex virus (HSV) type 1 encephalitis is described that is based on the selective uptake by infected cells of radiolabeled antiviral drug, consisting of 5-substituted 1-(2'-deoxy-2'-substituted .beta.-D-arabinofuranosyl)pyrimidine

nucleoside, and external scanning by positron emission tomog. or gamma scanning. For example, female CD rats infected with HSV-1 were administered [2-<sup>14</sup>C]FMAU

(2'-fluoro-5-methyl-1- $\beta$ -D-arabinofuranosyl[2-<sup>14</sup>C]uracil) (47.5  $\mu$ Ci/mg). <sup>14</sup>C activity in infected regions exceeded background in all HSV-1 infected rats. FMAU showed rapid blood clearance and was excreted mainly in unchanged form. The organ distribution of [2-<sup>14</sup>C]FMAU in HSV-1 infected rats is presented. Suitable labels for use in positron emission tomog. or gamma scanning are discussed.

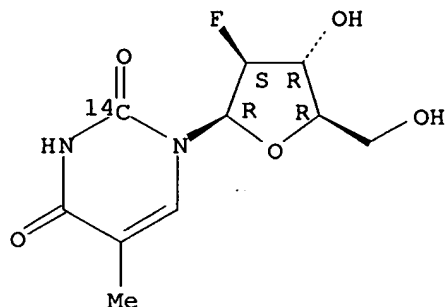
IT 83374-60-1

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metab. of, in herpes simplex virus type 1 encephalitis, positron tomog. or scintigraphy in relation to)

RN 83374-60-1 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione-2-<sup>14</sup>C, 1-(2-deoxy-2-fluoro- $\beta$ -D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 99 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:105771 HCAPLUS

DOCUMENT NUMBER: 102:105771

TITLE: Sensitivity of arabinosyladenine-resistant mutants of herpes simplex virus to other antiviral drugs and mapping of drug hypersensitivity mutations to the DNA polymerase locus

AUTHOR(S): Coen, Donald M.; Fleming, H. Edward, Jr.; Leslie, Laurel K.; Retondo, Margaret J.

CORPORATE SOURCE: Dep. Pharmacol., Harvard Med. Sch., Boston, MA, 02115,

USA

SOURCE: J. Virol. (1985), 53(2), 477-88

CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Seven herpes simplex virus mutants which have been previously shown to be resistant to arabinosyladenine [5536-17-4] were examd. for their sensitivities to 4 types of antiviral drugs. These drugs were a pyrophosphate analog, 4 **nucleoside** analogs altered in their sugar moieties, 2 **nucleoside** analogs altered in their base moieties, and 1 altered in both. The 7 mutants exhibited 5 distinct phenotypes based on their sensitivities to the drugs relative to wild-type

strain KOS. All mutants exhibited resistance to acyclovir [59277-89-3] and arabinosylthymine [605-23-2], as well as marginal resistance to iododeoxyuridine [54-42-2], whereas all but one exhibited resistance to phosphonoformic acid [4428-95-9]. The mutants exhibited either sensitivity or hypersensitivity to the other drugs tested, 2'-nor-deoxyguanosine [82410-32-0], 5-methyl-2'-fluoroarauracil [69256-17-3], 5-iodo-2'-fluoroarauracil [69123-98-4], and bromovinyldeoxyuridine [82768-44-3], some of which differed only slightly

from drugs to which the mutants were resistant. These results suggest ways to detect and treat arabinosyladenine-resistant isolates in the clinic. Antiviral hypersensitivity was a common phenotype. Mutations conferring hypersensitivity to 2'-nor-deoxyguanosine in mutant PAAr5 and to bromovinyldeoxyridine in mutant tsD9 were mapped to nonoverlapping regions of 1.1 and 0.8 kilobase pairs, resp., within the herpes simplex virus DNA polymerase [9012-90-2] locus. Thus, viral DNA polymerase mediates sensitivity to these 2 drugs. However, reports of mutations in the DNA polymerase locus conferring resistance to these 2 drugs could not be confirmed. All of the mutants exhibited altered sensitivity to .gtoreq.2 types of drugs, suggesting that single mutations affect recognition of the base, sugar, and triphosphate moieties of nucleoside triphosphates by viral polymerase.

IT 69256-17-3

RL: BIOL (Biological study)

(herpes simplex virus hypersensitivity to, arabinosyladenine resistance

and DNA polymerase gene in relation to)

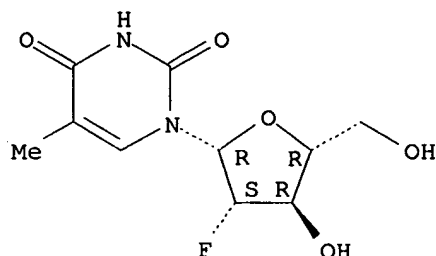
RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-

5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 100 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1985:39537 HCAPLUS

DOCUMENT NUMBER: 102:39537

TITLE: Cell-specific antiviral activity of  
1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-  
iodocytosine (FIAC) against Marek's disease  
herpesvirus and turkey herpesvirus

AUTHOR(S): Schat, Karel A.; Schinazi, Raymond F.; Calnek, Bruce  
W.

CORPORATE SOURCE: New York State Coll. Vet. Med., Cornell Univ.,  
Ithaca,

NY, 14853, USA

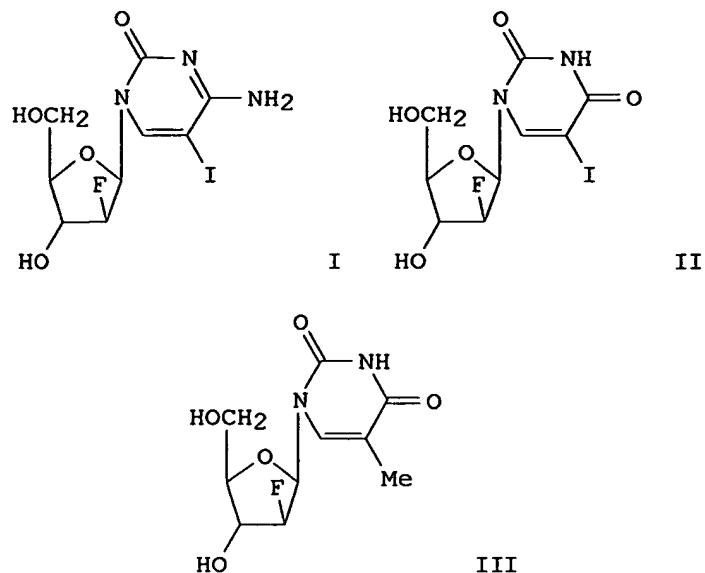
SOURCE: Antiviral Res. (1984), 4(5), 259-70

CODEN: ARSRDR; ISSN: 0166-3542

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Three new fluoroarabinosylpyrimidine nucleosides [1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) (I) [69123-90-6], 1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-iodouracil (FIAU) (II) [69123-98-4], and 1-(2-fluoro-2-deoxy-.beta.-D-arabinofuranosyl)-5-methyluracil (FMAU) (III) [69256-17-3]] were tested for in vitro activity against oncogenic and nononcogenic strains of Marek's disease virus (MDV) and herpesvirus of turkeys (HVT). Marek's disease is a herpesvirus-induced lymphoma in chickens. Nononcogenic strains of MDV and

HVT can protect against this disease. All viruses were inhibited by 1 .mu.M of these drugs in chick kidney cell (CKC) cultures, but only FMAU and FIAU were active in chicken embryo fibroblast (CEF) and spleen cell cultures. It was detd. that whereas CKC produced the enzyme 2'-deoxycytidine-deaminase [37259-56-6] which is needed to deaminate

FIAC

to FIAU, CEF were devoid of this enzyme activity. In addn., the deaminase inhibitor 3,4,5,6-tetrahydrouridine prevented the antiviral activity of FIAC and CKC. FMAU was not active against two Marek's disease-derived lymphoblastoid tumor cell lines.

IT 69256-17-3

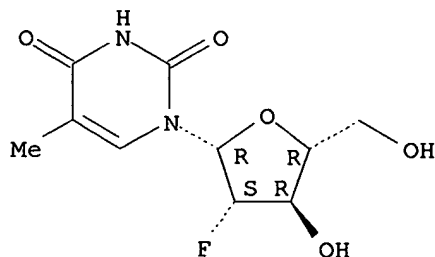
RL: BIOL (Biological study)

(Marek's disease and herpes virus infection prevention with)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

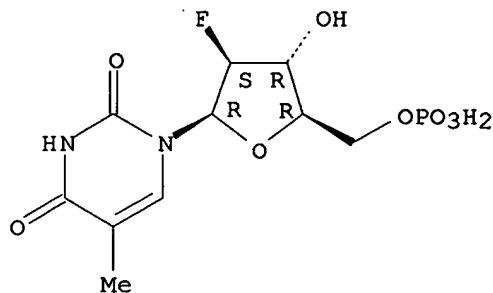
Absolute stereochemistry.





ACCESSION NUMBER: 1985:39529 HCAPLUS  
 DOCUMENT NUMBER: 102:39529  
 TITLE: Kinetics of the interaction of monophosphates of the  
 antiviral nucleosides 2'-fluoro-1-.beta.-D-  
 arabinofuranosylpyrimidine and  
 (E)-5-(2-bromovinyl)-2'-  
 deoxyuridine with thymidylate kinases from Vero cells  
 and herpes simplex virus types 1 and 2  
 AUTHOR(S): Chen, Ming S.; Amico, Leonard A.; Speelman, Dan J.  
 CORPORATE SOURCE: Pharm. Res. and Dev. Div., Bristol-Myers, Syracuse,  
 NY, 13221-4755, USA  
 SOURCE: Antimicrob. Agents Chemother. (1984), 26(5), 778-80  
 CODEN: AMACQ; ISSN: 0066-4804  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The affinities of the monophosphates of 2'-fluoro-5-iodo-1-.beta.-D-  
 arabinofuranosyluracil and its 5-Me analog for cellular thymidylate  
 kinase  
 [9014-43-1] were two or more orders of magnitude greater than for the  
 thymidine-thymidylate kinase [9002-06-6] from herpes simplex virus types  
 1 and 2. In contrast, the monophosphate of (E)-5-(2-bromovinyl)-2'-  
 deoxyuridine [80860-82-8] was found to have a higher affinity for the  
 viral enzymes than for the cellular enzyme.  
 IT 94344-82-8  
 RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)  
 (thymidylate kinase of herpes simplex virus response to)  
 RN 94344-82-8 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-2-fluoro-5-O-phosphono-.beta.-D-  
 arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d 111 102-115 ibib abs hitstr

L11 ANSWER 102 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1984:566417 HCAPLUS  
 DOCUMENT NUMBER: 101:166417  
 TITLE: The inhibition of ultraviolet radiation-induced DNA  
 repair in human diploid fibroblasts by  
 arabinofuranosyl nucleosides  
 AUTHOR(S): Snyder, Ronald D.; Van Houten, Bennett; Regan, James  
 D.  
 CORPORATE SOURCE: Stauffer Chem. Co., Farmington, CT, 06032, USA  
 SOURCE: Chem.-Biol. Interact. (1984), 50(1), 1-14  
 CODEN: CBINA8; ISSN: 0009-2797  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The antiviral compds. 9-.beta.-D-arabinofuranosyladenine (ara-A),  
 9-.beta.-D-arabinofuranosyl-2-fluoroadenine (FAA), 9-.beta.-D-

arabinofuranosylhypoxanthine (ara-Hx), 9-.beta.-D-arabinofuranosylguanine (ara-G), 1-.beta.-D-arabinofuranosylthymine (ara-T), 1-.beta.-D-arabinofuranosyl-2'-fluorocytosine (FAC), 1-.beta.-D-arabinofuranosyl-2'-fluoro-5-iodocytosine (FIAC), and 1-.beta.-D-arabinofuranosyl-2'-fluoro-5-methyluracil (FMAU) were compared to 1-.beta.-D-arabinofuranosyl cytosine (ara-C) in their ability to inhibit UV light-induced DNA repair in log phase and confluent human diploid fibroblasts. Inhibition of the polymn. or ligation steps of DNA excision repair manifests itself in the form of DNA single-strand breaks which may be quantitated through velocity sedimentation anal. in alk. sucrose gradients. In UV-irradiated quiescent, confluent human fibroblast cultures, treatment with any of the arabinucleosides leads to accumulation of single-strand breaks but the ED for this inhibition varies greatly. The order of their effectiveness in confluent cultures was ara-C and its derivs. >ara-A, FAA, ara-G, Ara-HX > ara-T. In rapidly cycling cells, on the other hand, sensitivity to

repair inhibition was exhibited only in response to ara-C and FAC. If 2 mM hydroxyurea (HU) was administered with ara-A, FAA, or FMAU, however, DNA strand breaks were seen. HU also increased the efficiencies of ara-C and FAC. No strand breaks were obsd. in UV-irradiated log-phase cells

treated with FIAC, ara-Hx, ara-G, or ara-T even in the presence of HU. The efficiencies of inhibition of unscheduled DNA synthesis (UDS) and semiconservative DNA synthesis by the arabinucleosides is consistent with their relative efficiencies at producing strand breaks. The ability of the arabinucleosides to inhibit DNA is discussed with respect to their hypothesized effects on DNA metabolic processes in eukaryotic cells.

IT 69256-17-3

RL: BIOL (Biological study)

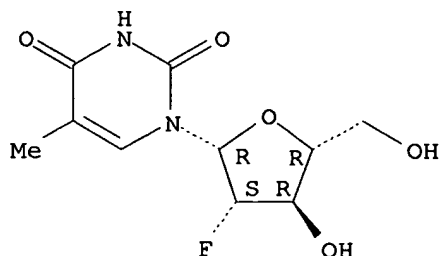
(DNA repair in human fibroblasts induction by UV radiation inhibition by)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 103 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1984:64869 HCAPLUS

DOCUMENT NUMBER: 100:64869

TITLE: Effects of certain **nucleoside** analogs on human cytomegalovirus replication in vitro

AUTHOR(S): Mar, Engchun; Patel, Pravin C.; Cheng, Yungchi; Fox, Jack J.; Watanabe, Kyoichi A.; Huang, Engshang

CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA

SOURCE: J. Gen. Virol. (1984), 65(1), 47-53

CODEN: JGVIAY; ISSN: 0022-1317

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Four **nucleoside** analogs, 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluracil (I), -5-iodouracil (II),

-5-methylcytosine (III) and -5-iodocytosine (IV), were studied for their effect on human cytomegalovirus (HCMV) replication in vitro. I, II, III, and IV showed antiviral activities for 4 strains of HCMV (Major, Clegg, D550 and Towne) in a plaque redn. assay, with ED50s in the range of 0.1-0.65 .mu.M. At 1 .mu.M I or IV, the synthesis of 5 virus-specific late polypeptides was entirely blocked. Quantification of Towne viral

#### DNA

synthesis, using complementary RNA-DNA hybridization with a

#### Towne-specific

cRNA probe, demonstrated a complete inhibition of HCMV DNA replication at 1 .mu.M I or IV. After the removal of the inhibitors, however, viral DNA synthesis resumed, and infectious virus reappeared, indicating that the inhibition of HCMV replication by these **nucleoside** analogs was of a virostatic reversible type.

#### IT 69256-17-3

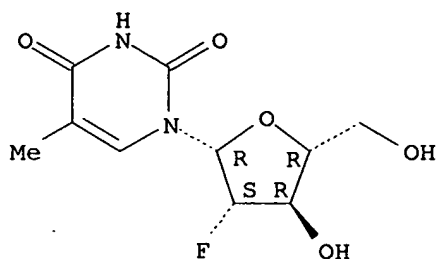
RL: BIOL (Biological study)

(human cytomegalovirus replication inhibition by)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 104 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1984:48296 HCAPLUS

DOCUMENT NUMBER: 100:48296

TITLE: Alterations in the recognition of **nucleoside** analogs as substrates by the deoxythymidine kinase of a 5-methoxymethyldeoxyuridine-resistant mutant of herpes simplex virus type 1

AUTHOR(S): Veerisetty, V.; Veerisetty, Indira K.; Gentry, Glenn A.

CORPORATE SOURCE: Med. Cent., Univ. Mississippi, Jackson, MS, 39216, USA

SOURCE: J. Gen. Virol. (1983), 64(12), 2767-70

CODEN: JGVIA Y; ISSN: 0022-1317

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhibition consts. (Kis) were used as an est. of the ability of various **nucleoside** analogs to be recognized as substrates by the deoxythymidine kinases (dTKs) of a 5-methoxymethyldeoxyuridine-resistant (MMdUr) mutant of herpes simplex virus type 1 (HSV-1) and its parent wild-type (wt). The Kis for the 5-position analogs MMdU, [E]-5-(2-bromovinyl)deoxyuridine, bromodeoxyuridine, and iododeoxyuridine were increased approx. 3-5-fold, suggesting that they were poorer substrates for the MMdUr dTK than for the wt dTK. With the 2' analogs arabinosylthymine and 2'-fluoro-5-methylarabinosyluracil, however, the

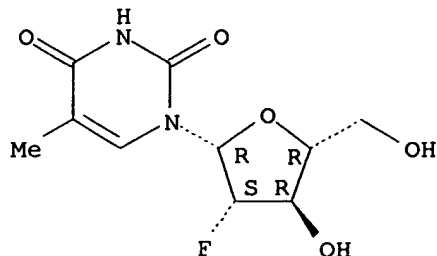
Kis were increased to a much greater extent, 80- and 240-fold, resp. These findings suggest that the resistance of the mutant MMdUr to these analogs may be due to a mutation(s) in the viral dTK that directly affects

binding

at the 2' recognition site and indirectly at the 5, while still allowing

substantial activity with the natural substrate deoxythymidine.  
 IT **69256-17-3**  
 RL: BIOL (Biological study)  
 (as substrate, deoxythymidine kinase of methoxymethyldeoxyuridine-resistant mutant of herpes simplex virus recognition of)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

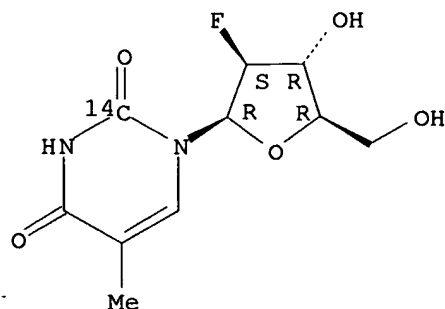
Absolute stereochemistry.



L11 ANSWER 105 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1983:609169 HCAPLUS  
 DOCUMENT NUMBER: 99:209169  
 TITLE: Prospects for the use of radiolabeled antiviral drugs  
 in the diagnosis of herpes simplex encephalitis  
 AUTHOR(S): Price, Richard W.; Saito, Yutaka; Fox, Jack J.  
 CORPORATE SOURCE: Cotzias Lab. Neuro-Oncol., Meml. Sloan-Kettering  
 Cancer Cent., New York, NY, 10021, USA  
 SOURCE: Biochem. Pharmacol. (1983), 32(17), 2455-61  
 CODEN: BCPCA6; ISSN: 0006-2952  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The title method is described and discussed. As an example, rats were  
 intraocularly inoculated with herpes simplex encephalitis type 1 and i.v.  
 injected with carbon-14-labeled 2'-fluoro-5-methyl-1-.beta.-D-  
 arabinosyluracil (I); brains were then removed and in-vivo uptake of I  
 was  
 detected by autoradiog. with computer reconstruction as described by Y.  
 Saito et al. (1982). Although improvements are still needed, this method  
 is potentially useful for early specific diagnosis of herpes simplex in  
 humans by various in-vivo scanning methods.

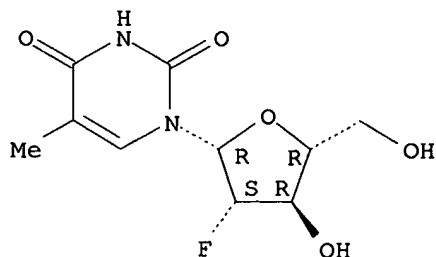
IT **83374-60-1**  
 RL: ANST (Analytical study)  
 (for diagnosis of herpes simplex encephalitis)  
 RN 83374-60-1 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione-2-<sup>14</sup>C, 1-(2-deoxy-2-fluoro-.beta.-D-  
 arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



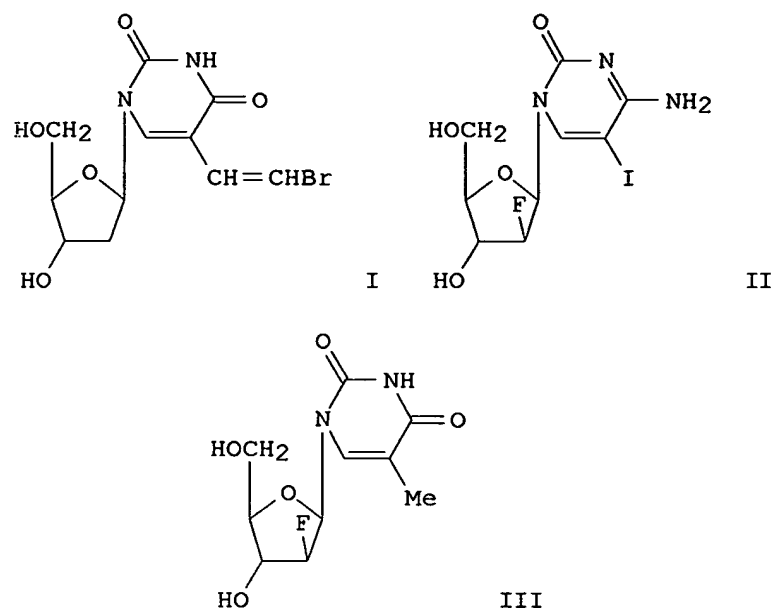
L11 ANSWER 106 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1983:605677 HCAPLUS  
 DOCUMENT NUMBER: 99:205677  
 TITLE: Efficacy and selectivity of some nucleoside analogs as antihuman cytomegalovirus agents  
 AUTHOR(S): Colacino, Joseph M.; Lopez, Carlos  
 CORPORATE SOURCE: Lab. Herpesvirus Infect., Sloan-Kettering Inst. Cancer  
 SOURCE: Res., New York, NY, 10021, USA  
 Antimicrob. Agents Chemother. (1983), 24(4), 505-8  
 CODEN: AMACQJ; ISSN: 0066-4804  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 1-(2'-Deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-iodocytosine (FIAC) [69123-90-6], 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-methyluridine (FMAU) [69256-17-3], 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-iodouridine (FIAU) [69123-98-4], and 1-(2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-5-ethyluridine (FEAU) [83546-42-3] were evaluated for antiviral activities against human cytomegalovirus (HCMV) and compared with 9-[(2-hydroxyethoxy)methyl]guanine (acyclovir) [59277-89-3] and E-5-(2'-bromovinyl)-2'-deoxyuridine (BVDU) [69304-47-8]. The relative anti-HCMV potencies of these compds., as detd. by calcg. the dose of drug which inhibited 50% plaque formation, were in order of decreasing potency:  
 FIAC > FIAU > FMAU > acyclovir > FEAU > BVDU. The antiviral activity of FIAC occurred at levels much lower than those that caused cytotoxic or cytostatic effects in uninfected fibroblasts. Neither thymidine nor deoxycytidine reversed the anti-HCMV activity of FIAC, indicating that this drug was not acting as an analog of the natural nucleosides. FIAC was not phosphorylated by cytosols of HCMV-infected cells to a greater extent than by those of uninfected cells, indicating that, unlike the antiviral activity against herpes simplex virus type 1, the selectivity of this drug is probably not based on a virus-specified pyrimidine kinase.  
 IT 69256-17-3  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (virucidal activity of, against humans cytomegalovirus)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 107 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1983:515621 HCAPLUS  
 DOCUMENT NUMBER: 99:115621  
 TITLE: Epstein-Barr virus: inhibition of replication by three new drugs  
 AUTHOR(S): Lin, Jung Chung; Smith, M. Carolyn; Cheng, Yung Chi; Pagano, Joseph S.

CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC,  
27514, USA  
SOURCE: Science (Washington, D. C., 1883-) (1983), 221(4610),  
578-9  
CODEN: SCIEAS; ISSN: 0036-8075  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB Acyclovir [59277-89-3], the first clin. useful drug effective against replication of Epstein-Barr virus (EBV) was without effect against latent or persistent EBV infection. Three **nucleoside** analogs, E-5-(2-bromovinyl)-2'-deoxyuridine (I) [69304-47-8], 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-iodocytosine (II) [69123-90-6] and 1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-methyluracil (III) [69256-17-3] were potent inhibitors of EBV replication in vitro. Moreover, in contrast to the reversibility of viral inhibition by acyclovir, these 3 drugs have prolonged effects in suppressing viral replication even after the drugs are removed from persistently infected cell cultures.

IT 69256-17-3

RL: BIOL (Biological study)

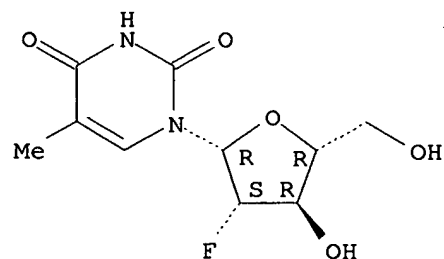
(Epstein-Barr virus replication inhibition by)

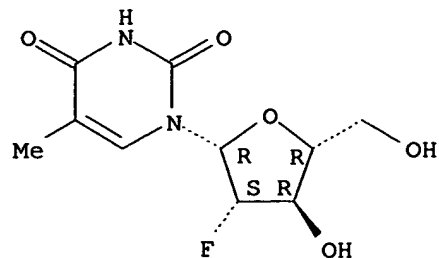
RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(2-deoxy-2-fluoro-β-D-arabinofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

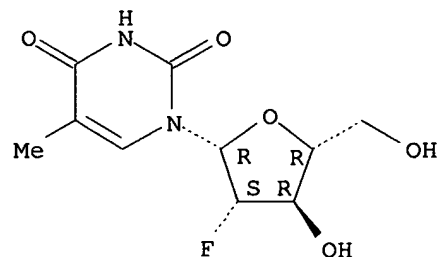
Absolute stereochemistry.





L11 ANSWER 108 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1983:154910 HCAPLUS  
 DOCUMENT NUMBER: 98:154910  
 TITLE: Structure-activity relationship of ligands of the pyrimidine **nucleoside** phosphorylases  
 AUTHOR(S): Niedzwicki, John G.; El Kouni, Mahmoud H.; Chu, Shih Hsi; Cha, Sungman  
 CORPORATE SOURCE: Div. Biol. Med., Brown Univ., Providence, RI, 02912, USA  
 SOURCE: Biochem. Pharmacol. (1983), 32(3), 399-415  
 CODEN: BCPA6; ISSN: 0006-2952  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Eighty-seven pyrimidine base and **nucleoside** analogs were evaluated as inhibitors of uridine phosphorylase (UrdPase) [289-95-2] and thymidine phosphorylase (dThdPase) [9030-23-3]. These findings, together with an extensive literature review, have allowed construction of structure-activity relationships for the binding of ligands to UrdPase and dThdPase and provide a basis for the rational design of new inhibitors of these enzymes. Addnl., 2,6-pyridinediol [626-06-2] and 6-benzyl-2-thiouracil [6336-50-1] were identified as being potent inhibitors of UrdPase and dThdPase, resp.  
 IT **69256-17-3**  
 RL: BIOL (Biological study)  
 (pyrimidine **nucleoside** phosphorylase inhibition by, structure in relation to)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

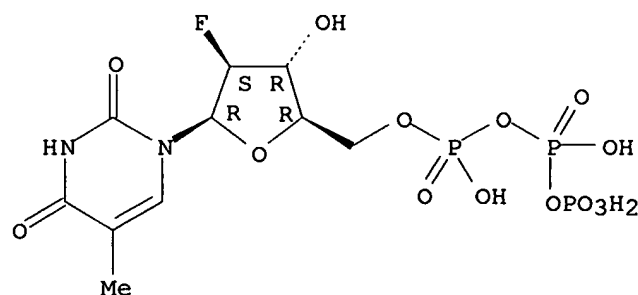
Absolute stereochemistry.



L11 ANSWER 109 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1982:484821 HCAPLUS  
 DOCUMENT NUMBER: 97:84821  
 TITLE: Differential effect of **nucleoside** analog triphosphates on ribonucleotide reductases from uninfected and herpes simplex virus-infected HeLa

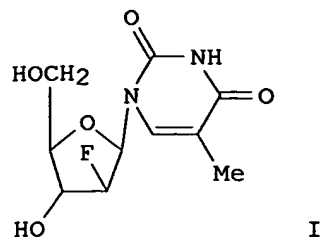
cells  
 AUTHOR(S): Nakayama, Koji; Ruth, Jerry L.; Cheng, Yung C.  
 CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC,  
 27514, USA  
 SOURCE: J. Virol. (1982), 43(1), 325-7  
 CODEN: JOVIAM; ISSN: 0022-538X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of the triphosphates of 8 pyrimidine nucleoside  
 analogs (5-substituted, 2'-fluoroara-, and acyclonucleosides) and  
 acycloguanosine were examd. on ribonucleotide reductase [9040-57-7]  
 prepd. from uninfected and herpes simplex virus types 1- and 2-infected  
 HeLa cells. Of the analogs tested, E-5-propenyl- [79551-91-0] and  
 E-5-(2-bromovinyl)-dUTP [77222-61-8] were more potent inhibitors of the  
 enzyme from virus-infected cells than was dTTP [365-08-2]. In  
 uninfected  
 cells acyclo-TTP [82617-27-4] was the most effective inhibitor. The  
 results are discussed in relation to the antiviral activities of the  
 analogs.  
 IT 79551-89-6  
 RL: BIOL (Biological study)  
 (ribonucleotide reductase from uninfected and herpes simplex  
 virus-infected HeLa cells response to)  
 RN 79551-89-6 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-  
 [hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-  
 arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 110 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1982:466080 HCAPLUS  
 DOCUMENT NUMBER: 97:66080  
 TITLE: Activity of 2-fluoro-5-methylarabinofuranosyluracil  
 against mouse leukemias sensitive to and resistant to  
 1-.beta.-D-arabinofuranosylcytosine  
 AUTHOR(S): Burchenal, J. H.; Chou, T. C.; Lokys, L.; Smith, R.  
 S.; Watanabe, K. A.; Su, T. L.; Fox, J. J.  
 CORPORATE SOURCE: Mem. Sloan-Kettering Cancer Cent., New York, NY,  
 10021, USA  
 SOURCE: Cancer Res. (1982), 42(7), 2598-600  
 CODEN: CNREA8; ISSN: 0008-5472  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI

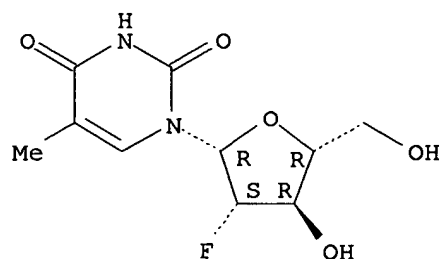




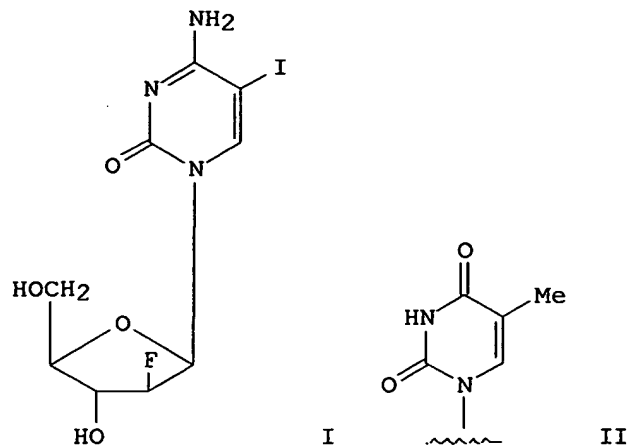
AB A new pyrimidine nucleoside, 2'-fluoro-5-methyl-1- $\beta$ -D-arabinofuranosyluracil (I) [69256-17-3] was active against mouse and human leukemic cells in culture and against mouse leukemias L1210, P388, and P815 in vivo. In contrast to other 1- $\beta$ -D-arabinofuranosylcytosine (ara-C) [147-94-4] derivs., I, when given either i.p. or orally, was highly active against lines of leukemias P815 and L1210 made resistant to ara-C. Against P815/ara-C and L1210/ara-C, it is more effective than is 5-azacytidine, a drug which has shown definite effectiveness in patients with acute leukemia resistant to ara-C. Thus, I may be useful in treatment of ara-C resistant leukemias.

IT 69256-17-3  
 RL: BIOL (Biological study)  
 (leukemia inhibition by, ara-C resistance in relation to)  
 RN 69256-17-3 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione,  
 1-(2-deoxy-2-fluoro- $\beta$ -D-arabinofuranosyl)-  
 5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 111 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1982:85896 HCAPLUS  
 DOCUMENT NUMBER: 96:85896  
 TITLE: 2'-Fluoroarabinosyl pyrimidine nucleosides:  
 chemistry, antiviral, and potential anticancer  
 activities  
 AUTHOR(S): Fox, J. J.; Lopez, C.; Watanabe, K. A.  
 CORPORATE SOURCE: Mem. Sloan-Kettering Cancer Cent., Sloan-Kettering  
 Inst., New York, NY, USA  
 SOURCE: Med. Chem. Adv., Proc. Int. Symp., 7th (1981),  
 Meeting  
 Date 1980, 27-40. Editor(s): De las Heras, Federico  
 G.; Vega, Salvador. Pergamon: Oxford, Engl.  
 CODEN: 46NHAC  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English  
 GI



AB A series of 2'-fluoro-5-substituted-arabinofuranosyl-cytosines and -uracils were prepd. Two of these I and II, were found to be very potent and highly selective against herpes simplex virus (HSV) types 1 and 2 at very low drug levels. Cytotoxicity to uninfected Vero or human fibroblast

cell proliferation was minimal. The selectivity of I against HSV vs. its low cytotoxicity against Vero cells is due, at least in part, to a virus-specified thymidine kinase. Structure-activity studies demonstrate

that the 2'-fluoro substituent in the up (arabino) configuration is essential for this potent antiviral activity. Substitution of the 2'-fluoro group by chloro or bromo reduces the antiviral potency. I is also active in a plaque redn. assay against herpes zoster virus at concn. of 0.01  $\mu$ M and against cytomegalovirus plaque formation at 0.1  $\mu$ M. In vivo studies in mice inoculated with 20 LD<sub>50</sub> of HSV-1 show that I and II are effective, the latter giving 60% cures at dose levels as low as 1 mg/kg/day x5. The selective cytotoxicity of I against human tumor cell lines but not against normal human cells is discussed.

IT **69256-17-3P**

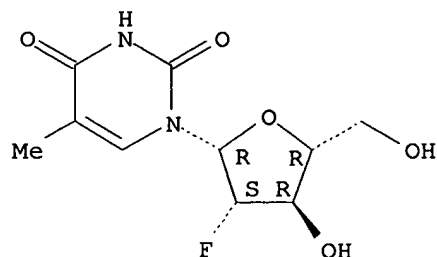
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and virucidal activity of)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,

1-(2-deoxy-2-fluoro- $\beta$ -D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 112 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1981:614866 HCAPLUS

DOCUMENT NUMBER: 95:214866

TITLE: **Nucleoside** analogs with clinical potential  
in antivirus chemotherapy. The effect of several  
thymidine and 2'-deoxycytidine analog

5'-triphosphates

simplex

AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

DOCUMENT TYPE:

LANGUAGE:

GI

on purified human (.alpha., .beta.) and herpes

virus (types 1, 2) DNA polymerases

Ruth, Jerry L.; Cheng, Yung Chi

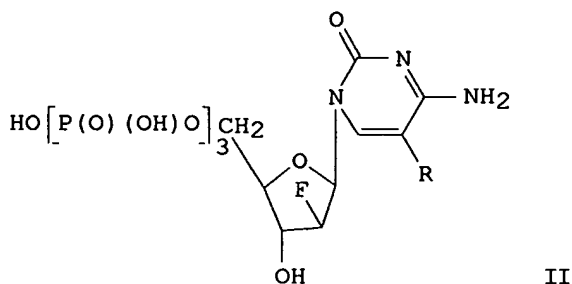
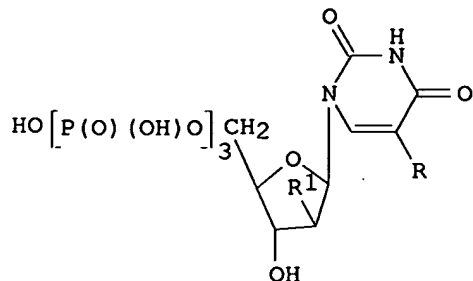
Cancer Res. Cent., Univ. North Carolina, Chapel Hill,  
NC, 27514, USA

Mol. Pharmacol. (1981), 20(2), 415-22

CODEN: MOPMA3; ISSN: 0026-895X

Journal

English



AB To aid in establishing the mechanisms of antiherpes virus action and the basis for selectivities of 7 **nucleoside** analogs, I (R = Me, Pr, CH:CHMe, or CH:CHBr, R1 = H or OH) and II (R = Me or I) were prepd. for testing with DNA polymerase [9012-90-2]; a general method for the direct chem. synthesis of **nucleoside** triphosphate from **nucleoside** is described. The effects of the analog triphosphates were evaluated on the following 4 isolated DNA polymerases: virus-induced DNA polymerases from herpes simplex virus Type 1 (HSV-1) and Type 2 (HSV-2) infections, and human DNA polymerases .alpha. and .beta., using conditions optimal for each. Competitive inhibition results indicate

that

all 7 analog triphosphates are good inhibitors of normal substrate utilization by DNA polymerase regardless of enzyme source, have much higher apparent affinities (20- to 600-fold lower Ki) for HSV polymerases than for human polymerases, and are equally inhibitory to both HSV-1 and HSV-2 DNA polymerases. The analogs varied considerably in support of DNA synthesis in the absence of normally competing substrate, again with little difference between polymerases. The relative ability to support DNA synthesis was generally E-5-propenyl-dUTP [79551-91-0] .simeq. dTTP

>

E-5-(2-bromovinyl-dUTP) [77222-61-8] > 5-propyl-dUTP [64374-76-1] .mchgt. 2'-fluoro-arabinonucleoside triphosphates .mchgt.

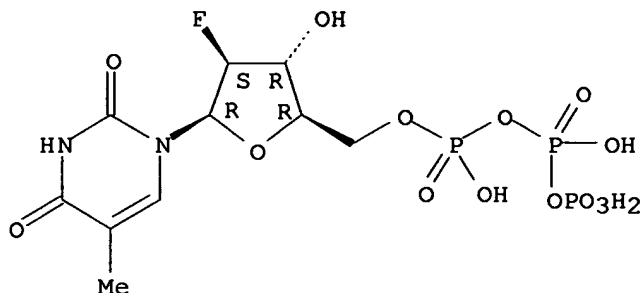
E-5-(2-bromovinyl)-araUTP [79551-90-9]. Incubation of analog triphosphates and polymerase with activated DNA suggests that, with E-5-(2-bromovinyl)-araUTP as the exception, the analogs have little

effect

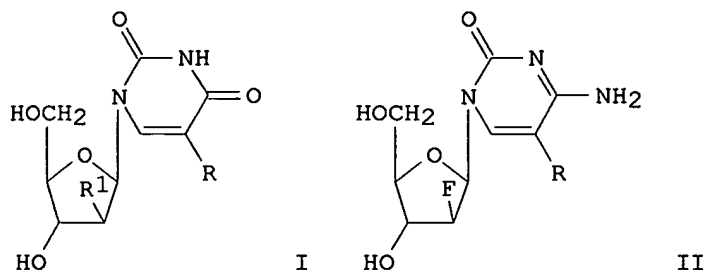
on the subsequent ability of product DNA to serve as primer template. E-5-Propenyl-dUTP exhibited behavior the most similar to dTTP throughout these studies. Some general structure-activity relationships are

discussed.  
 IT 79551-89-6  
 RL: BIOL (Biological study)  
 (DNA polymerase inhibition by, antiviral activity in relation to)  
 RN 79551-89-6 HCAPLUS  
 CN 2,4(1H,3H)-Pyrimidinedione, 1-[2-deoxy-2-fluoro-5-O-  
 [hydroxy[[hydroxy(phosphonooxy)phosphinyl]oxy]phosphinyl]-.beta.-D-  
 arabinofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 113 OF 115 HCAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1981:580671 HCAPLUS  
 DOCUMENT NUMBER: 95:180671  
 TITLE: Differential activity of potential antiviral  
**nucleoside** analogs on herpes simplex  
 virus-induced and human cellular thymidine kinases  
 AUTHOR(S): Cheng, Y. C.; Dutschman, G.; Fox, J. J.; Watanabe, K.  
 A.; Machida, H.  
 CORPORATE SOURCE: Cancer Cent., Univ. North Carolina, Chapel Hill, NC,  
 27514, USA  
 SOURCE: Antimicrob. Agents Chemother. (1981), 20(3), 420-3  
 CODEN: AMACQJ; ISSN: 0066-4804  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB The rates of phosphorylation of the potential antiviral **nucleoside**  
 analogs I (R = I, Me, CH:CHBr; R1 = H, F, OH) and II (R = I, Me) by  
 purified thymidine kinase [9002-06-6] from both human and herpes simplex  
 virus sources were studied. Most of the analogs were phosphorylated by  
 both human and viral kinases. The analogs were competitive inhibitors of  
 thymidine phosphorylation by the kinases; on the assumption that  
 inhibition const. (Ki) reflect binding affinity, Ki values of the  
 analogs  
 were detd. In general, the analogs have a greater affinity for the viral  
 kinases than for the human kinases. The amt. of the analogs  
 phosphorylated to the monophosphate form, which is presumably necessary

for cytotoxic activity, was dependent on both the phosphorylation rates and binding affinities. All of the analogs act as preferential substrates for the viral kinases at low concns., which may be one of the main reasons for their selective antiviral action. The structure-activity relations of the analogs are discussed.

IT 69256-17-3

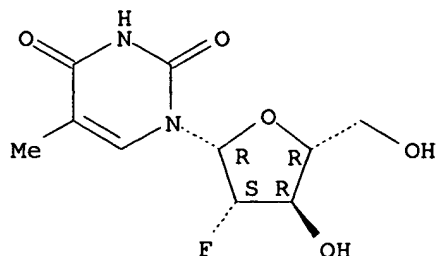
RL: BIOL (Biological study)

(phosphorylation of, by thymidine kinase, structure and virucidal activity in relation to)

RN 69256-17-3 HCAPLUS

CN 2,4(1H,3H)-Pyrimidinedione,  
1-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-  
5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 114 OF 115 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1981:561687 HCAPLUS

DOCUMENT NUMBER: 95:161687

TITLE: Pharmacological disposition and metabolic fate of 2'-fluoro-5-iodo-1-.beta.-D-arabinofuranosylcytosine in mice and rats

AUTHOR(S): Chou, Ting-Chao; Feinberg, Aaron; Grant, Alan J.; Vidal, Pedro; Reichman, Uri; Watanabe, Kyoichi A.; Fox, Jack J.; Philips, Frederick S.

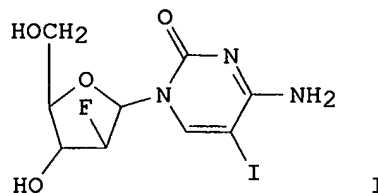
CORPORATE SOURCE: Lab. Pharmacol., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA

SOURCE: Cancer Res. (1981), 41(9, Pt. 1), 3336-42  
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB 2'-Fluoro-5-iodo-1-.beta.-D-arabinofuranosylcytosine-HCl (FIAC) (I) [69123-90-6] was synthesized and labeled with <sup>14</sup>C in the 2 position for the study of pharmacol. disposition and metabolic fate. FIAC is deaminated by cytosine nucleoside deaminase [9025-06-3] at a rate comparable to that of 1-.beta.-D-arabinofuranosylcytosine. The deaminated product, 2'-fluoro-5-iodo-1-.beta.-D-arabinofuranosyluracil (FIAU) [69123-98-4] is, like FIAC, an active antiviral agent. After i.v.